US PATENT APPLICATION
Docket No. WILB01

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS & INTERFERENCES

Application of: BRIAN R. WILL

Serial No. 10/608,408 Examiner: Shay
Filed: June 27, 2003 Group Art Unit: 3739

For: EYE FIXATION APPARATUS

Date: December 15, 2008

BRIEF OF THE APPELLANT -

APPLICANT, BRIAN R. WILL, M.D.

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REAL PARTY IN INTEREST

Applicant, Brian R. Will, is the real party in interest to this appeal.

RELATED APPEALS AND INTERFERENCES

No other appeals or interferences relate to the instant appeal.

STATUS OF CLAIMS

Claims 1-22 are pending.

Claims 1-22 were rejected under § 112 second paragraph for indefiniteness based upon Applicant's use of the term "convex" in the claims.

Claim 22 was rejected under § 112 second paragraph for indefiniteness based upon Applicant's use of the terms "low profile" and recitation of the element "the profile of the eye fixation portion is substantially narrow" in the claim.

Claims 1, 11, and 12 were finally rejected under 35 U.S.C. § 103(a) as unpatentable over EP0372127A1 to L'Esperance (hereinafter "L'Esperance") or US6,042,594 to Hellenkamp (hereinafter "Hellenkamp").

Claims 2 and 13 were finally rejected under § 103(a) as unpatentable over L'Esperance or Hellenkamp as applied to claims 1, 11 and 12, and further in combination with US4,173,980 to Curtin (hereinafter "Curtin").

Claims 3/1, 3/2, 4/3/1, 4/3/2, 7/4/3/1, 7/4/3/2, 8/7/4/3/1, 8/7/4/3/2, 14-16, 18 and 19 were finally rejected under § 103(a) as unpatentable over L'Esperance or Hellenkampf as applied to claims 1, 11 and 12, and further in combination with Curtin or US5,591,174 to Clark et al (hereinafter "Clark").

Claims 5/3/1, 5/3/2, 6/4/3/1, 9/7/4/3/1, 9/7/4/3/2, 10/8/7/4/3/1, 10/8/7/4/3/2, 17 and 20-22 were finally rejected under § 103(a) as unpatentable over L'Esperance or Hellenkamp in combination with Curtin and Clark as applied to claims 3/1, 3/2, 4/3/1, 4/3/2, 7/4/3/1, 7/4/3/2, 8/7/4/3/1, 8/7/4/3/2, 14-16, 18 and 19, and further in combination with US5,613,061 to Olson et al (hereinafter "Olson").

STATUS OF AMENDMENTS.

Prior to this Response, an Office Action rejecting all claims was mailed July 11, 2008, responding to Applicant's RCE which included an affidavit submission with accompanying references under 37 C.F.R. 1.132, dated April 14, 2008. Examiner repeated the final rejections made in the office action prior to the RCE. Applicant timely filed an Amendment After Final Rejection concurrently with a Notice of Appeal with applicable fees on October 14, 2008. Applicant has not received any notice regarding entry or refusal to enter the after-final amendments. Applicant appeals all rejections.

Claims 2-10 and 13 are original. Claims 14-21 were previously amended. Claim 22 was presented in the prior RCE. Claims 1, 11, 12 and 22 were amended after final rejection and concurrent with the filing of the Notice of Appeal.

Claim 12 was amended to correct an informality which referred to a singular antecedent claim in plural. Claim 12 was amended to read:

> 12. The method of claims 11, further comprising:
>
> checking to see said eye fixation apparatus is centered around the cornea; and
>
> shutting off the vacuum pressure if said eye fixation apparatus is not centered around the cornea, recentering said eye fixation apparatus, and reapplying said vacuum pressure.

No new matter was added thereby and the amendment created no change in claim scope.

Claims 1-22 were rejected under § 112 second paragraph for indefiniteness based upon Applicant's use of the term "convex" in the claims. Independent Claims 1, 11 and 22 were amended after Final Rejection to address Examiner's arguments regarding the use of "convex" in the claim language and thereby reduce the issues to be addressed on appeal. The amendments are indicated in the Claims Appendix. Specifically, Claim 1 was amended to read:

> 1. An eye fixation apparatus, comprising:
>
> an eye fixation portion, wherein the eye fixation portion has an annular convex bottom contact portion, said convex bottom contact portion including a concave bottom surface, which goes upon the surface of an eyeball and encircles the cornea, and wherein the contact portion bottom surface is provided with criss-crossing channels; and
>
> a vacuum port connected to said eye fixation portion and in communication with said criss-crossing channels such that vacuum pressure applied to said vacuum port exerts vacuum pressure through such criss-crossing channels to pull the eyeball membrane to the criss-crossing channels.

Claim 11 was amended to read:

> 11. A method of fixating an eye cornea for surgery, comprising:
>
> placing an eye fixation apparatus upon the eye globe conjunctiva around the cornea, wherein the eye fixation apparatus comprises an eye fixation portion with an annular convex bottom contact portion, said convex bottom contact portion including a concave bottom surface, provided with criss-crossing channels, and a vacuum port connected to said eye fixation portion and in communication with said criss-crossing channels such that vacuum pressure applied to said vacuum port exerts vacuum pressure through such criss-crossing channels to pull the eyeball membrane to the criss-crossing channels; and
>
> applying vacuum pressure to said vacuum port creating a pressure differential through said criss-crossing channels in relation to said conjunctiva, adhering said conjunctiva to said contact portion bottom surface.

Claim 22 was amended to read:

> 22. An eye fixation apparatus, comprising:
>
> an eye fixation portion, wherein the eye fixation portion has a low-profile annular convex bottom contact portion, said convex bottom contact portion including a concave bottom surface, which goes upon the surface of an eyeball and encircles the cornea, and wherein the contact portion bottom

surface is provided with criss-crossing channels;

a vacuum port connected to said eye fixation portion and in fluid communication with said criss-crossing channels;

a first annular translation guide member with a first translation rod and first adjustment knob, adjustably connected to the eye fixation portion, wherein the first translation guide member portion can translate laterally in relation to the eye fixation portion using said first adjustment knob acting upon said first translation rod;

a second annular translation guide member with a second translation rod and second adjustment knob, adjustably connected to the first translation guide member, wherein the second translation guide member portion can translate laterally in relation to the first translation guide member and eye fixation portion using said second adjustment knob acting upon second first translation rod;

a first and a second docking screw screwed through said first and second translation guide members, respectively, and for tightening the first and second translation guide members against objects inserted into the cylindrical space formed by the first and second annular translation guide members; and

wherein, the profile of said eye fixation portion is substantially narrow so as to fit under the eye lid of a patient without use of a lid speculum.

Support for the amendments is found in the Specification at p.6, ll. 6-9: "...

and on the bottom provided with an annular convex contact portion 14 *which is shaped to conform to the surface of the eye globe* and to encircle the cornea." (Emphasis added). Specific support is also found in Figs. 1, 3 and 4, clearly showing a contact portion which is convex from the outside, but which therefore includes a concave interior surface which conforms to the shape of an eyeball. Support is also found in the Specification at pp. 1-4, in the Background and Summary and Advantages, discussing the advantages of the claimed device in reducing deformation of the cornea and eyeball and reducing rises in intraocular pressure. Based on the Specification and Drawings, a person of ordinary skill in the art would clearly have understood that a convex bottom contact portion which is shaped to conform to the surface of the eye globe includes a concave interior surface which is in contact with the corneal surface. There could be no confusion as to the scope of the claims based on the use of "convex". However, Applicant has amended the claims with more explicit language in order to narrow the issues on appeal. No new matter is added thereby, and no change in claim scope is created by the amendments.

The claims, as amended, are reproduced in the Claims Appendix to this Brief.

SUMMARY OF CLAIMED SUBJECT MATTER

Means or step plus function analysis section. Applicant does not argue any of the pending claims as means- or step-plus-function claims.

Summary of claimed subject matter.

The present invention relates generally to devices and methods for fixating eyes for ophthalmic surgery, and more particularly to eye fixation devices and methods using vacuum pressure for fixation for guiding a surgical tool or laser.

Claims 1-10 relate to a novel apparatus for fixating the eye. Independent claim 1 recites an eye fixation apparatus having an contact portion with criss-crossing vacuum channels and a vacuum portion in communication with the criss-crossing channels. *Specification p.6-7, ll. 6-3; Figs. 1, 3, 4, #12, 14, 16, 18.* The bottom contact portion is convex to match the convex profile of the cornea. *Specification p.6, ll. 6-9; Fig. 4, #14.* The interior surface of the eye fixation portion contacts the corneal surface via the lands between criss-cross vacuum distribution channels by pulling the corneal surface toward the vacuum channels. *Specification p.6, ll. 17-20; p.11, ll. 8-19; Figs. 1, 3, 4, #14, 16.*. A vacuum port is provided in communication with the criss-crossing channels to draw the eyeball membrane to the channels. *Specification p. 6, ll. 14-17; p. 7, ll. 13-17; p.11,*

ll. 8-19; Fig.1, 3, #18. .

Claims 2-9 depend from claim 1. Claim 2 includes adjustment arms which allow the surgeon to use both hands to adjust the eye fixation device in relation to the eyeball before applying vacuum, or to readjust if not correctly aligned after the first application of vacuum. *Specification p. 7, ll. 18-21; Figs. 1, 2, 5, #20.*

Claims 3, 4, 7 and 8 include first and second annular translation guide members, and translation rods with adjustment knobs, allowing the surgeon to adjust the annular opening, which is what receives surgical instruments or allows application of a surgical laser, normally in relation to one another (e.g. in a perpendicular X-Y direction), after applying vacuum to fix the fixation apparatus to the eyeball. *Specification pp. 7-10, ll. 23-18; Figs. 1, 2, 5, 6, #22, 24, 26, 28, 40, 44, 52, 56, 60, 64, 66, 68, 70.* The threaded guide rods allow precise adjustment of position to fine tune the initial positioning of the device. *Id.*

Claims 5, 6, 9, and 10 include docking screws through the first and/or second annular translation guide members so that surgical devices, such as laser sighting cones, can be inserted and locked into the annular opening, thereby fixing the surgical devices to the eyeball rather than the eyeball being forced to align with the devices. *Specification pp. 10-11, ll. 19-2;*

p.11, ll. 14-19; Figs. 1, 2, 5, # 72.

Claim 22 is an apparatus claim in independent claim format which incorporates the limitations of Claims 1-10 and explicitly recites a narrow profile which fits under a patient's lid without need for a lid speculum. *Specification p. 3, ll. 6-19; p. 4, ll. 11-21; Figs. 3, 4, #14.*

Independent Claim 11 recites a method for using a novel apparatus having an annular convex bottom contact portion provided with criss-crossing vacuum channels to provide fixation of the eyeball during ophthalmic surgeries, including the steps of placing an eye fixation apparatus around the cornea and applying vacuum to the vacuum channels to fixate the eyeball. . *Specification p.6-7, ll.6-3; p.11, ll. 8-19; Figs. 1, 3, 4, #12, 14, 16, 18.* Claims 12-21 depend from claim 11.

Claim 12 further includes the steps of verifying the centering of the eye fixation apparatus and adjusting if necessary by shutting off vacuum, recentering the device, and re-applying vacuum pressure. *Specification pp. 6-7, ll. 20-3; p. 11, ll. 12-14.*

Claim 13 includes the methods of claims 11 or 12 where the apparatus includes adjustment arms. *Specification p. 7, ll. 18-21; p. 11, ll. 8-19; Figs. 1, 2, 5, #20*

Claims 14 and 18 include the methods of claims 11 or 12 wherein the

apparatus includes X and/or Y translation guide members. *Specification pp. 7-10, ll. 23-18; p. 11, ll. 8-19; Figs. 1, 2, 5, 6, #22, 24, 26, 28, 40, 44, 52, 56, 60, 64, 66, 68, 70.*

Claims 15 and 19 include the methods of claims 14 and 18, wherein the X and Y translation guide members are provided with threaded adjustment rods and knobs for fine adjustment. *Specification pp. 7-10, ll. 23-18; p. 11, ll. 8-19; Figs. 1, 2, 5, 6, #22, 24, 26, 28, 40, 44, 52, 56, 60, 64, 66, 68, 70.*

Claims 16, 17, 20 and 21 include the methods of claims 14, 15, 18 or 19, wherein the X and/or Y translation guide members are provided with docking screws. *Specification pp. 10-11, ll. 19-2; p.11, ll. 8-19; Figs. 1, 2, 5, # 72.*

SUMMARY OF EVIDENCE OF RECORD

Applicant has submitted significant evidence of record supporting a conclusion of non-obviousness, including two affidavits and several articles from peer reviewed scientific medical journals. The evidence is reproduced in the attached Evidence Appendix. The following is a summary of the evidence of record.

Affidavit of Dr. Brian Will dated January 10, 2007, and Exhibit

The first affidavit of Dr. Will, the Applicant, is dated January 10, 2007, and will be referred to as "*First Will Aff.*" Dr. Will laid the foundation for his description of the prior and differences between the claimed invention and the prior art, as well as the problems solved by his invention.

Dr. Will is a board certified Ophthalmologist with over 17 years of practice, having performed over 28,000 LASIK procedures as well as over 10,000 other ocular procedures in that time, and currently perform over 3,000 LASIK procedures per year. He has intimate experience with much of what has been considered state of the art in the field of LASIK and other keratome procedures, using lasers and microkeratome blades, including the devices incorporating the Hellenkamp (U.S. 6,042,594), Clark (U.S. 5,591,174), Curtin (U.S. 4,173,980) and L'Esperance (E.P. 0372127A1) references, or similar to these references, cited by the Examiner. This

declaration is made based on my personal experience and that of my staff of two (2) ophthalmologists within the field. Dr. Will explained the novel features of his claimed invention solve problems associated with prior art devices such as described in Hellenkamp, Clark, Curtin and L'Esperance.

As explained by Dr. Will, an important aspect of the claimed apparatus and methods is the criss-cross vacuum channel of the eye-fixation portion. The criss-cross channel provides several specific advantages over the prior art. The lands between the channels provide multiple contact points spread over a wider surface, preventing the cornea, sclera and conjunctiva from being displaced into the vacuum channels and providing a more stable contact. The criss-cross channels prevent occlusion of the vacuum source during surgical procedures. The criss-cross channels markedly reduce deformation of the eye and reduce intraocular pressure – thus it is safer, more comfortable, and provides improved accuracy, especially in Femtosecond procedures. Criss-cross allow a lower profile device compared to vacuum annulus devices, obviating need for a lid speculum. Criss-cross channels allow a surgeon to reposition the fixation device, whereas vacuum annulus devices prevent repositioning due to corneal damage. Criss-cross channels permit rapid and thorough cleaning of the apparatus.

Other claimed aspects of the invention provide additional important advantages over the prior art. X-Y translation guides, see dependent claims 3-10 and 14-21, provide adjustment capabilities built in to the fixation device which allow for superior centration properties in laser procedures, whereas prior art devices do no provide for adjustment on the fixation device itself. The addition of docking screws, see dependent claims 5, 6, 9, 10, 16, 17, 19, 20 and 21, for docking surgical devices into the fixation aperture, rather than conventional pincer type docking systems, provide smoother docking with less manual dexterity required by the surgeon.

The criss-cross channel design, claims 1 and 11, allows a lower vacuum setting to achieve the same fixation of the eye, and the narrowness and cross-orientation prevent significant displacement of the cornea, sclera and conjunctival tissue into the vacuum channels. Existing annular vacuum rings, such as taught by the Hellenkamp and Curtin references cited by the Examiner, displace significant amounts of tissue into the vacuum ring cavity, causing distortion of the eyeball, changes to the thickness of the cornea and lens, and unnecessary damage to the corneal tissues. Porous membrane devices such as described in L'Esperance are easily - inevitably - clogged by mucous, which can create an unbreakable vacuum seal that would damage the cornea when attempting to disengage it.

The criss-cross channels recited as an element of all claims reduce the potential for trauma to the cornea, a leading cause of post-LASIK complications. The incidence of subconjunctival hemorrhage has been estimated as high as 10% or more in LASIK patients. *First Will Aff.* ¶ *7.*

The low profile achieved by the criss-cross channel design eliminates the need for a lid speculum in most cases, including patients with narrow ocular fissures and orbits. Higher rates of complications from using annular fixation devices on patients with narrow ocular fissures and orbits has been documented in medical studies. *First Will Aff.* ¶ *8 (a copy of the referenced article was included for Examiner as Exh. 5 to Second Aff. Will and is included in the Evidence Appendix).* Dr. Will discussed a peer-reviewed journal article along with the First Will Affidavit noting higher rates of complications for patients with narrow ocuolar fissures, in this case patients of Asian desent. *First Will Aff.* ¶ *7.*

The pores of the L'Esperance design are quite vulnerable to clogging – as is the case with any porous membrane applied to mucus surfaces. I have found, based on extensive experience in thousands of surgical procedures, that devices such as that taught by L'Esperance have at least two major drawbacks that are not mere "speculation." First, L'Esperance relies on applying suction through a porous surface backed by an annular chamber.

The porous surface is subject to clogging by mucus from the conjunctiva surface – all porous surfaces are subject to clogging, which can cause loss of suction, locked in suction, and cross contamination. A second drawback of the L'Esperance reference, shared by other references cited by the Examiner, is the high profile of the vacuum chamber vault necessitated by annular designs, which requires use of lid specula for many patients which can lead to complications and discomfort.

The X-Y translation capability built in to the eye fixation apparatus, (claims 3-10 and 14-21) and the use of docking screws rather than conventional pincers (claims 5,6, 9, 10, 16, 17, 20 and 21), are also major improvements over the state of the art. The X-Y adjustment capability allows the laser or other surgical apparatus to be slaved to the eyeball, rather than vice versa (e.g. as shown in the Curtis reference, cited by the Examiner). Use of translation rods with adjustment knobs, directly on the eye fixation device, greatly reduces the manual dexterity required for adjustments, and provides for more accurate docking of the surgical apparatus.

The x-y translation capability of claims 3-10 and 14-21 allows the surgeon to dock the laser or other apparatus into the fixation device, and

make simple adjustments using the docking screws (claims 5,6, 9, 10, 16, 17, 20 and 21) while sighting to an eye with minimal distortions.

The addition of adjustment arms, as in claims 2, 13 and 22 allow a surgeon to easily maneuver the device on the eye surface without their fingers obscuring their vision. Additionally, because the surgeon's fingers are holding the adjustment arms – i.e. away from the actual conjunctival surface – there is less chance of scratches or contamination due to inadvertent contact.

Affidavit of Dr. Brian Will dated April 14, 2008, and Exhibits.

The second affidavit of Dr. Will is dated April 14, 2008, and will be referred to as the "*Second Will Aff.*" The Second Will Aff. was submitted to place evidence before the Examiner relating to the limitations of prior art devices, the differences between Applicant's invention and the prior art, and a longstanding need that has gone unsolved. In response to Examiner's argument denying that the annular vacuum ring fixation devices of the prior art, such as described in Hellenkamp, Clark and Curtin, caused complications and less-than-optimal patient outcomes (see *OA 07112008; OA 04112007*) Dr. Will submitted six peer reviewed journal articles as exhibits to the affidavit, which are reproduced in the Evidence Appendix.

Dr. Will stated that he has extensive experience in the field and what

would be considered the state of the art, both by conducting thousands of surgical procedures himself and through the supervision and training of his staff of board certified ophthalmologists. The articles demonstrated a growing concern with complications related to LASIK and other ophthalmological procedures, and that research into the causes demonstrated that annular vacuum ring type eye fixation apparatus were a significant cause of complications and/or less than optimal outcomes.

Exhibit 1 to the *Second Will Aff.* is a true and correct copy of an article, Jose L. Hernandez-Verdejo, Miguiel A. Teus, Jose M. Roman, Gema Bolivar, PORCINE MODEL TO COMPARE REAL-TIME INTRAOCULAR PRESSURE DURING LASIK WITH A MECHANICAL MICROKERATOME AND FEMTOSECOND LASER, *Investigative Ophthalmology & Visual Science*, January 2007, Vol. 48, No. 1. The intent of the authors was to compare the elevation of intraocular pressure (IOP) caused by the flap-cutting portion of LASIK procedures using a mechanical microkeratome blade versus laser microkeratome cutter. At page 1, the authors note that there is a widespread concern about the damage caused to eye structures from the increased IOP during LASIK and other procedures. The authors note that several hypothesis focus on the "suction ring" used to fix the eye during procedures. "Different hypotheses explain the posterior segment complications, with the

first postulating that the mechanical stress is caused by the IOP elevation produced by the pneumatic suction ring, which may induce tangential stress on the posterior segment." Id at p.68, col 2. The authors note that real-time measurement of changes in IOP during LASIK and other procedures have been difficult to measure in the past. Id. During the experimental procedures the IOP of the porcine eyeballs was recorded continuously. Id at p. 69, col 2. "Both groups [mechanical and laser flap cuts] had an IOP increase immediately after the placement of the suction ring that was maintained during the entire surgical procedure." Id p.70, col 2. The authors noted another study which demonstrated analogous significant rises is IOP using single-port versus two-port suction rings. Id at p.70, col 2. The authors' noted that "...pressure setting for the suction ring is an important variable in determining consistent corneal flap thickness during LASIK" and that lower vacuum settings tend to produce lesser increases in IOP. Id. pp. 70-71. "Sudden increases in IOP, although well tolerated, may induce changes in the peripheral retina... These possible posterior segment complications, among others, make the knowledge of the exact IOP increase induced by surgical procedures such as laser refractive surgery increasingly important." In the field of ophthalmologic surgical procedures the term "suction ring" is generally understood to refer to a vacuum annulus design,

essentially the same as taught in Hellenkamp. Vacuum annulus designs are the industry standard at this time.

Exhibit 2 to the *Second Will Aff.* is a true and correct copy of an article, Wei-Li Chen, Yung-Feng Shih, Shu-Lang Liao, Fung-Rong Hu, Por-Tying Hung, ULTRASOUND BIOMICROSCOPIC FINDINGS IN RABBIT EYES UNDERGOING SCLERAL SUCTION DURING LAMELLAR REFRACTIVE SURGERY, *Investigative Ophthalmology & Visual Science*, December 2002, Vol. 43, No. 12. The purpose of the study was to evaluate changes in corneal structure caused by changes in IOP due to application of scleral suction rings. Suction ring related complications during lamellar refractive surgeries (including LASIK) included retinal vascular occlusion, ischemic optic neuropathy, and macular hemorrhages due to elevated IOP during surgery, and subconjunctival hemorrhage – caused by application of the suction ring. *Id at 3669, col 1.* The authors concluded that the application of the suction ring itself causes harm to a subject's eye, and that the amount of damage correlated to the length of time the suction ring was applied. The damage was due to the stresses induced by the deformation of the eye itself and consequent rise in IOP, as well as the effect of the suction ring on the scleral surface displacing into the suction ring volume. *Id at pp. 3670-71.*

Exhibit 3 to the *Second Will Aff.* is a true and correct copy of an article, Alireza Mirshahi, MD, Thomas Kohnen, MD, EFFECT OF MICROKERATOME SUCTION DURING LASIK ON OCULAR STRUCTURES, *Ophthalmology*, April 2005, Vol. 112, No. 4. The purpose was, "To study the effect of microkeratome suction on ocular structures during LASIK." The procedures were conducted using a 20.3 mm suction ring. *Id at p.646, col 1.* "The mechanics of microkeratome suction can be compared to that of blunt ocular trauma when the ocular globe is compressed and quickly released... however, at a much lower level incidence and degree." *Id at p.648, col 2.* The authors noted that more study is required to understand the precise causes. Thus, this article corroborated Dr. Will's assertion that existing suction ring designs (as described in Hellenkamp, Clark and Curtin) are a source of trauma to the eyes of patients undergoing LASIK procedures. Applicant's invention addresses what Dr. Will asserts to be part of the cause of this trauma – the displacement of the sclera into the high chamber of suction ring designs such as Hellenkamp, and the deformation of the eyeball caused by these designs, which draw the eyeball up and into the central opening for cutting of the keratome flap.

Additionally, the authors describe increased IOP as desirable "creating a firm cornea and permitting a precise corneal flap to be cut, which

is followed by laser ablation." *Id at p.645*. This is in direct contrast to the present invention, which is designed to fix the eyeball while minimizing or eliminating IOP and achieves this through minimizing distortion of the corneal tissue. Thus, the conventional literature teaches directly away from Applicant's invention.

Exhibit 4 to the *Second Will Aff.* is a true and correct copy of an article, Christina J. Flaxel, MD, Young H. Choi, MD, Michael Sheety, MD, Stephen Christopher Oeinck, CRA, Joe Y. Lee, MD, Peter J. McDonnell, MD, PROPOSED MECHANISM FOR RETINAL TEARS AFTER LASIK, *Ophthalmology*, 2004; Vol. 111, pp. 24-27. The suction ring used in the study was described: "The suction ring is a circular chamber that fixates the eye by means of a vacuum. The underside of the fixation ring has a vacuum chamber that seals against the globe." *Id at p. 26, col. 1-2.* This matches the description of the devices in Hellenkamp, Curtin and Clark and is indicative of prior art devices. The authors concluded that the mechanics of the suction ring itself may be a source of damage to eyes of patients with pre-existing vulnerabilities.

Exhibit 5 to the *Second Will Aff.* is a true and correct copy of an article, Julie M. Albietz, PhD, Lee M. Lenton, Suzanne G. McLennan, DRY EYE AFTER LASIK: COMPARISON OF OUTCOMES FOR ASIAN AND

CAUCASIAN EYES, *Clinical and Experimental Optometry*, March 2005, vol 88.2. The purpose was to investigate anecdotal evidence that LASIK patients of Asian decent experienced higher incidences of complications such as Dry Eye after LASIK. The authors found that Asian LASIK patients did suffer higher incidence of dry eye, with several potential contributing causes. One cause discussed was the smaller ocular orbit and tighter lids generally found in Asian patients compared to Caucasian patients. *Id at p. 95*. The tighter lid structure led to a higher incidence of flap cut complications and longer intra-operative prep times leading to greater damage to the ocular surface were due in large part to the tight fit of the suction ring between the lids. *Id at p. 95*. One of the advantages of the low profile apparatus of the present Application is that it fits under the eyelids of patients. Thus, the lids must accommodate only the narrow central access hole for the microkeratome blade or laser access (approximately 9-12mm) rather than the full diameter of the vacuum ring (approximately 20mm +/-). *See Exhibit 3 to Second Will Aff., above*). Additionally, the longer intraoperative prep times required by the use of lid specula translates into longer application of vacuum to the suction ring, which as discussed in *Exh. 2 to Second Will Aff., above*, seems to lead to increased trauma to the ocular surface and anterior structures.

Attached as Exhibit 6 to the *Second Will Aff.* is a true and correct copy of an article, Jane-Ming Lin, MD, Yi-Yu Tsai, MD, RETINAL PHLEBITIS AFTER LASIK, *Journal of Refractive Surgery*, September/October 2005, Vol. 21, p.501. The authors provide a case study of a patient suffering retinal phlebitis due to LASIK complications. The authors concluded that the cause of the retinal phlebitis may have been due to the negative effects of elevated IOP caused in part by the suction ring. The authors note that standard practice is to achieve an IOP of at least 65mmHg to support mechanical keratome flap cutting. *Id at 502, col 2.* Again, this emphasis on intentionally raising IOP is directly opposite the goal of minimizing IOP increase in Applicant's invention.

The Exhibits discussed above, as a whole, demonstrate that the existing industry suction rings, which are essentially versions of those described in Hellenkamp and Curtin/Clark, are known to be problematic in LASIK procedures although this was not known at the time of the Hellenkamp reference. The present invention seeks to reduce the damage caused by suction ring devices such as described in Hellenkamp, which are commonly used in ophthalmologic surgery.

Regarding the porous membrane and high profile chamber of L'Esperance, Dr. Will explained that the porous membrane system of

L'Esperance would be subject to frequent clogging and be difficult or impossible to properly clean and sterilize. Dr. Will noted that in his 17 years of practice he had never come across a vacuum fixation device using the L'Esperance porous membrane system, which would imply a confirmation of the problems associated with L'Esperance. If the L'Esperance membrane were effective then surgeons would use it. The nature of the L'Esperance device also requires a high profile vacuum chamber. Therefore, all of the problems described, and which are supported in the professional literature, relating to high profile devices would apply especially to L'Esperance.

Dr. Will addressed the Examiner's prior stated skepticism regarding the need for lid specula when using high profile suction rings such as described in Hellenkamp, Curtin, Clark and L'Esperance. A high profile suction ring will actually not fit into many patients' eyes as their lid fissures are simply not large enough to accept the diameter or high profile vacuum ring required, which is especially true for patients of Asian descent and smaller people. With high profile apparatus described in Hellenkamp and L'Esperance the surgery either cannot be performed on such patients, or the patient must have their eyelids cut open and then sutured back together at the completion of the surgery. This significantly increases the risk of the surgeries, and leads to longer healing times for the patients.

Dr. Will described several of the negative effects of high profile devices such as Hellenkamp and L'Esperance. In many, many cases where the lids are very tight, although the surgery can be completed, the patient experiences excessive pain because the surgeon has to stretch the lid tissues in order to place the suction ring. This stretching may lead to permanent damage to the delicate lid tissue (skin, tendons and muscles) and result in development of "droopy" lids or redundant skin on the eyelids over the longer term. Such conditions would require additional surgery to repair. These are medical facts that any experienced refractive surgeon would be aware of and are outlined to the patient in every surgical consent form. In contrast, the low profile vacuum ring of the present Application allows much of the footprint of the vacuum fixation device to be inserted *under* the lids, thereby allowing surgery to be performed without these difficulties or long term risks. The low profile is achieved through the use of the criss-cross vacuum channels, which are elements of all claims.

Other problems with high profile suction rings, such as described in Hellenkamp and L'Esperance, lead to difficulties in carrying out the surgery itself. A high profile suction ring allows the patients' eyelids to gain more purchase, or force, on the ring. Patients that tend to squeeze their eyelids may dislodge the ring during the operation, which can result in irreversible

eye damage in the worst case. As a result, a lid speculum is nearly mandatory when using suction rings described in Hellenkamp and L'Esperance so as to control lid pressure. The low profile device described in the present Application causes a lower level of distention of the sidewall of the eye, so the patient will not likely feel the same level of pain or pressure and so will be less likely to squeeze their lids together (and therefore less likely to displace the suction ring and less likely to cause long term damage to the lid tissues). Equally important, the eye lids cannot obtain the same level of tension on the edge of the low profile vacuum ring and this markedly diminishes the need for a lid speculum and reduces the potential for serious intraoperative complications. The low profile device avoids this because eye lid slips comfortably over the vacuum footprint of the device.

The low profile of the claimed apparatus is achieved through the use of the criss-cross channel design. The criss-cross channels allow the use of shallower vacuum channels and distribute the vacuum over a greater area, allowing reduced vacuum levels. The Exhibits 1-6 to the *Second Will Aff.*, discussed above, all discuss the damage caused to the eye structures by higher vacuum applied through suction rings similar to Hellenkamp.

Examiner-cited Article

Examiner cited an article (Jose M. Benitez-del-Castillo, M.D., et al, DECREASE IN TEAR SECRETION AND CORNEAL SENSITIVITY AFTER LASER IN SITU KERATOMILEUSIS, *Cornea*, January 2001, Vol. 20, pp. 30-32), which is reproduced in the Evidence Appendix as Exhibit 3. The article is not relevant to any issue relating to the rejections. The study described in the article merely confirmed that dry eye is a known complication after LASIK procedures, and that artificial tears are a viable treatment in many cases. The study did not investigate causation but merely confirmed the correlation between LASIK procedures and dry eye. The study did not investigate abnormal outcomes or complications from LASIK outside typical dry eye symptoms.

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

All rejections are appealed by Applicant. Specifically:

1. Whether claims 1-22 are indefinite under § 112 second paragraph, for use of the term "convex"?

2. Whether claim 22 is indefinite under § 112 second paragraph, for use of the terms "low profile" or "the profile of the eye fixation portion is substantially narrow"?

3. Whether claims 1 and 11 are unpatentable under § 103(a) over L'Esperance or Hellenkamp?

4. Whether claim 12 is unpatentable under § 103(a) over L'Esperance or Hellenkamp?

5. Whether claims 2 and 13 are unpatentable under § 103(a) over L'Esperance or Hellenkamp in combination with Curtin?

6. Whether claims 3 and 14 are unpatentable under § 103(a) over L'Esperance or Hellenkamp in combination with Curtin or Clark?

7. Whether claims 7 and 18 are unpatentable under § 103(a) over L'Esperance or Hellenkamp in combination with Curtin or Clark?

8. Whether claims 4, 8, 15 and 19 are unpatentable under § 103(a) over L'Esperance or Hellenkamp in combination with Curtin or Clark?

9. Claims 5, 6, 9, 10, 17 and 20-22 under § 103(a) over L'Esperance or Hellenkamp in combination with Curtin or Clark, and Olson?

ARGUMENT

All arguments raised herein were raised with the Examiner in Applicant's responses to office actions or in the amendment after final rejection submitted concurrently with the Notice of Appeal.

THE SECTION 112 REJECTIONS

It is improper to reject a claim as indefinite where the scope of the claim (i.e. the metes and bounds of what would constitute infringement) would be understood by a person of ordinary skill in the art based on the claim as a whole when read in light of the Specification and Drawings. The mere fact that a claim could have been better worded does not render the claim indefinite. Metabolite Labs, Inc. v. Lab. Corp. of Am. Holdings, 370 F.3d 1354, 1366 (Fed. Cir. 2004) ("Only when a claim remains insolubly ambiguous without a discernible meaning after all reasonable attempts at construction must a court declare it indefinite.") Even under the more restrictive standard of patentability announced in *Ex Parte* Miyazaki, Appeal No. 2007-3300 (BPAI Nov. 19, 2008), the recitations of the claims are not "amenable to two or more plausible claim constructions." A claim construction that reads the preferred embodiment out of the scope of the

claims is not a "plausible" construction. Miyazaki, p. 11.[1] "Patentees are allowed much latitude in terminology and the language they use will be given the meaning intended by them if it can be ascertained from the context. It is immaterial that we must refer to the specifications for an understanding [of the claim recitals]." Lincoln Stores, Inc. v. Nashua Mfg. Co., 157 F.2d 154, 158 (1st Cir. 1946) (internal citations omitted). "It is settled law that the claims of a patent in order to be valid must define the patented invention with sufficient clarity that the metes and bounds thereof can be determined, but this requirement that the invention be pointed out with particularity does not preclude some latitude in claim interpretation, particularly where the meaning of what otherwise may be confusing recitals in the claims can be ascertained as here by referral to the specification and drawings." Kenmode Mfr. Co. v. U.S., 347 F.2d 315 (Ct. Cl. 1965) (internal citations omitted).

[1] Although Applicant cites Miyazaki as BPAI precedent, Applicant objects contending that the indefiniteness standard in Miyazaki violates binding Federal Circuit and Supreme Court precedent, and is inconsistent with the statutory requirements for patentability under 35 U.S.C. § 112, second paragraph. Nothing in the Patent Act, nor in higher court precedent, permits a different standard of patentability to applied by the USPTO as opposed to courts. The higher standards imposed by the presumed validity of an issued patent under 35 U.S.C. § 282 go to evidentiary standards and shifting burdens of persuasion, rather than statutory standards of patentability, as asserted in the Miyazaki decision. However, Applicant asserts that the rejections for indefiniteness must be reversed under either standard.

A non-standard use of a term is not indefinite if the meaning is clear when read in light of the Specification and Claims. Application of Mercier, 515 F.2d 1161, 1168-9 (C.C.P.A. 1975).

> "Assuming, arguendo that the phrase 'fluidized catalyst' is more often than not used to refer to a gas-suspended catalyst system, it does not follow that confusion will result when the phrase is used in a claim to refer to a finely divided catalyst in a dispersed or suspended state in a liquid phase. Whether a term used in a claim is conventional is not necessarily controlling on the question of indefiniteness. Since we are unable to see why or how there would be uncertainty over the plain meaning of the claim read in its entirety in view of the quoted portion which provides that the reaction mixture is in a liquid phase, the section 112 second paragraph rejection must be reversed."

Id. (Internal citations omitted.) The requirement for specificity requires only that the claim be as specific as the subject matter permits. Orthokinetics, Inc. v. Safety Travel Chairs, Inc., 806 F.2d 1565, 1576 (Fed. Cir. 1986) ("The claims were intended to cover the use of the invention with various types of automobiles. That a particular chair on which the claims read may fit within some automobiles and not others is of no moment. The phrase 'so dimensioned' is as accurate as the subject matter permits, automobiles being of various sizes." (Internal citations omitted.))

A. Claims 1-22: The term "convex" is clearly understood.

The Examiner rejected claims 1-22 under § 112 second paragraph stating that Applicant has misused the term "convex." *OA 07112008 at p.9.* As an initial matter, the Examiner never raised issue with this term in the prosecution of the application until after Applicant's submission of the first RCE, in an Office Action dated 04112007, so Applicant submits the use of the term is (and was) clearly understood. *See OA 09072005* (no mention of confusion over "convex"); *OA 07142006* (no mention of confusion over "convex"). The Examiner's dictionary definition of "convex" as "curved or rounded like the exterior of a sphere", *see OA 07112008 at p.9* is not incorrect, but the issue raised by the Examiner is simply one of orientation – a convex object may include a concave interior surface from the reverse perspective so they are not mutually exclusive. The "bottom portion" of the fixation device is convex, *see claims 1, 11 and 22, Figs. 1, 3, 4 #14,* although the bottom *surface* may be concave. The eyeball is essentially a ball – not perfectly spherical – i.e. convex. The eye fixation apparatus described in the application includes an "annular convex bottom contact portion" – i.e. annular to include an opening for access by a surgeon, and convex to match the convex contours of the eyeball. It necessarily follows that the inside of a convex annulus will be concave – it is merely a matter of

reference point. So reference to convex in this context, with reference to an eyeball, the Specification, the drawings, and the knowledge of a person of ordinary skill in the art, obviously would understand that one could refer to the overall shape as convex or concave and render the same meaning. As the Examiner raised this issue only after having numerous exchanges and discourses with Applicant via office actions without confusion, Applicant submits that "convex" as used in the Specification, Drawings and Claims is clear. Applicant presented these arguments to the Examiner. *See RCE 04142008 at pp.10-11.* Applicant, however, amended the claims after final rejection to specifically refer to the "concave contact surface", so this rejection should now be moot, *see claims 1, 11 and 22.*

Convex also is elucidated by reference to the Specification explaining that the eye fixation portion is low profile in order to fit under the patient's eyelids, so as to obviate the need for a lid speculum to hold back the eyelid. Thus, the "bottom contact portion" of the "eye fixation portion" is convex, so as to match the convex curvature of the eyeball and fit under the eyelids, whereas the inside surface of the "bottom contact portion" is concave. This is clear when the claim language is read in light of the Specification and Drawings as required. An object can be both convex and concave simultaneously, it is merely a matter of reference point, which reference

point is provided by the Specification and Drawings.

In Miyazaki, the BPAI refused to read in limitations from the disclosed preferred embodiment into the claims in order to find them definite. Here, however, there is no need to read in limitations from the preferred embodiment to render the claims definite, but rather the Examiner is attempting to impose a limitation into the claims which would render the preferred embodiment outside of the claim scope. Moreover, the issue is not one of narrowing or altering the definition of a word, but rather simply orientation when using the word. An object that is convex from the outside is concave on the inside. Describing the object as convex is therefore not ambiguous. Moreover, the Examiner is attempting to define "convex" in isolation from the wording of the entire claim itself. The claim language recites "... an annular convex bottom contact portion which goes upon the surface of an eyeball and encircles the cornea..." Construing this language as requiring a convex exterior shape as well as a convex interior surface is simply not plausible based on the plain claim language. The Examiner's proffered construction is even less plausible when read in light of the Specification and Drawings. There is no "plausible alternative meaning" in this case, as required under the Board's heightened standard of definiteness. Miyazaki, pp. 10-11.

Notably, the rejected claims include precisely that which the BPAI found lacking in the Miyazaki decision where "because the relative position of the user and printer are not well-defined in the claim, the claimed height of the paper feeding unit does not present a structural limitation on the height at all." Miyazaki, pp. 15-16. In stark contrast, claims 1, 11 and 22 recite a convex eye fixation part "...which goes upon the surface of an eyeball and encircles the cornea..." Therefore, the orientation of "convex" vs "concave" used by the Applicant is clear from the context and not subject to other *plausible* interpretations.

The only plausible reading is that "convex" refers to the shape from an external perspective, because a convex interior surface could not "[go] upon the surface of an eyeball". Applicant, however, has amended the claims to remove this issue from the appeal, adding a specific reference to the interior surface of the bottom contact portion.

B. Claim 22: "low profile" and "the profile of the eye fixation portion is substantially narrow" are clearly understood.

The Examiner rejected claim 22 under § 112 second paragraph stating that "low profile" is unclear as the total height of the device, including the X-Y translation guide members, would be too high to fit under an eyelid. Applicant submits the Examiner misreads the claim. *OA 07112008 at p. 9.*

It is the "eye fixation portion" which specifically includes the "low profile... substantially narrow so as to fit under the eye lid of a patient without the use of a lid speculum." *See Claim 22.* The claim does not recite that the entire device fits under a patient's eyelid, but merely the portion extending outward with the criss-cross vacuum channels - the "annular convex contact portion 14" is bottom portion which fixes the eye by applying vacuum to the criss-crossing channels. *See claim 22; Specification at p.6, ll. 6-9; Figs.1, 3, 4, #14.*

The Examiner misconstrues the reference to "profile" as requiring the vertical torroidal portion, which provides access for surgical instruments and can provide attachment points for X and Y translation guide members, to fit under the eye lid is incorrect when read in light of the Specification and Drawings. The Examiner's reliance on the measured proportions of Fig. 4 (*see OA 07112008 at p.9*) ignores the fact that such drawings and figures are not to scale but are necessarily distorted to enable reference to particular features. The Specification specifically points this lack of scale out. *See Specification, p.5, ll. 17-22.* The Examiner's measurements of the figures provided is therefore not applicable.

The need for a lid speculum is obviated in the present invention because the bottom contact portion, which is what grips the surface of the

eyeball, does not require a hollow annulus above that portion in order to distribute vacuum along the surface area contacting the eye. *See Specification at p.4, ll.11-13; First Aff. Will ¶8; Second Will Aff. ¶¶14-18.* This allows the eyelids to close to a degree over this thin lip, shown as # 14, in Fig. 4. The central open portion of the annulus which provides the access for surgical instruments and additional elements such as the translation guide members and docking screws, is sized to accept the surgical apparatus – which is essentially fixed. Prior art devices, such as L'Esperance (*see Fig. 1*), Hellenkamp (*see Fig. 2*) and Curtin (*see Fig. 2*), cited by the Examiner under 103(a) rejections, require a vertical vacuum annulus over the contact area as well as the central vertical annulus providing surgical access. It is this vacuum annulus of prior art devices which is eliminated by the use of criss-cross channels which can extend laterally through a thin extending lip. Applicant made this clear through the Specification, and more so through his affidavit which described in detail the problems caused by prior art devices and how the present invention solves these problems through the use of low profile criss-cross channels. See Specification at p. 3 ll. 8-10 describing the need for a "low profile fit[ting] comfortably under the eye lid"; and at p. 4 ll. 12-14 describing an advantage of the present device as being low profile and not requiring need for a lid speculum, thereby distinguishing the present

invention from existing devices.

Section 112 paragraph 2 requires the claims to be sufficiently clear to enable a person to understand, in light of the Specification and Drawings, what the applicant regards as the invention. This does not impose a requirement to provide detailed dimensions, but allows the use of relative dimensions or references, so long as they are adequately clear. The use of language such as "substantially narrow" in relation to a reference which provides basis by which a person of ordinary skill in the art can understand the structure as in "so as to fit under the eye lid of a patient without the use of a lid speculum" is sufficiently clear. *See* Orthokinetics, Inc. v. Safety Travel Chairs, Inc., 806 F.2d 1565, 1576 (Fed. Cir. 1986) ("A decision on whether a claim is invalid under § 112, 2d ¶, requires a determination of whether those skilled in the art would understand what is claimed when the claim is read in light of the specification.") Applicant submits that the claim, read in light of the specification and drawings, with the knowledge of a person of ordinary skill in the art, is clear and definite and has proper antecedent basis.

THE SECTION 103(A) OBVIOUSNESS REJECTIONS

The Examiner's rejections go beyond merely hindsight analysis and actually read teachings and elements into the cited prior art which are not

present under any reasonable reading of the references.

The standard under Section 103 is whether the claimed invention as a whole would have been obvious to a person of ordinary skill in the art at the time the invention was made. In re O'Farrell, 7 USPQ2d 1673, 1680 (Fed. Cir. 1988). "[A] patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." KSR Int'l v. Teleflex, Inc., 127 S.Ct. 1727, 1742, 167 L.Ed.2d 705 (2007). The Examiner bears the initial burden in the case of Section 103(a) obviousness rejection which requires the Examiner to put forward evidence that the invention as a whole would have been obvious to a person of ordinary skill in the art at the time of the invention. In re Piasecki, 745 F.2d 1468, 1472 (Fed. Cir. 1984) , citing In re Warner, 379 F.2d 1011, 1016 (CCPA 1967). Where the Examiner relies on a single prior art reference for an obviousness rejection, which does not describe every limitation of the claim, the Examiner must demonstrate how a person of ordinary skill in the art would have been motivated to modify the reference to achieve the invention without the benefit of hindsight, just as with a combination of references.

Where an Applicant submits evidence an Examiner cannot simply deny such evidence without citation to reference of submission of an

affidavit himself detailing the bases of his knowledge and expertise. MPEP 2142; In re Mayne, 41 U.S.P.Q.2d 1451, 1453 (Fed. Cir. 1997). Although the Supreme Court rejected rigid application of the "suggestion, motivation, teaching test" applied by courts in the past, it can still be a useful starting point for evaluation and to prevent hindsight analysis, so long as it is not applied rigidly and the evaluator maintains the framework of the analysis laid down in Graham v. John Deere Co., 383 U.S. 1 (1966). KSR, 127 S.Ct. at 1242. Moreover, the Examiner cannot rely on the applicant's disclosure in any way in making this *prima facie* case. MPEP 2143. The foundational facts for the *prima facie* case of obviousness are: (1) the scope and content of the prior art; (2) the difference between the prior art and the claimed invention; and (3) the level of ordinary skill in the art. Graham v. John Deere Co., 383 U.S. at 17-18; Miles Lab., Inc. v. Shandon Inc., 27 USPQ2d 1123, 1128 (Fed. Cir. 1993). Moreover, objective indicia such as commercial success and long felt need are relevant to the determination of obviousness. Stratoflex, Inc. v. Aeroquip Corp., 218 USPQ 231, 236 (Fed. Cir. 1983). Each obviousness determination rests on its own facts. In re Durden, 226 USPQ 359, 361 (Fed. Cir. 1985).

"It is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given

position to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one skilled in the art." Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc., 230 USPQ 416 (Fed. Cir. 1986). Here, the Examiner relies upon conclusory statements that combining the references "would be obvious to one of ordinary skill in the art." The Examiner thus failed to establish a *prima facie* case of obviousness to support rejection.

Further, regarding all of the § 103(a) rejections, the Examiner failed to make specific findings as to the level of ordinary skill and the differences between the prior art and the claimed invention.

No prior art references produced by the Examiner disclose an eye fixation apparatus with criss-crossing vacuum channels. Not individually. Not in any combination. The Examiner's rejections under Section 103 are based on the argument that criss-crossing vacuum channels are no different than a prior vacuum annulus ring (Hellenkamp, Curtis and Clark) or a flat porous membrane (L'Esperance) because these prior art devices are "presumed valid" and therefore work without flaws. The Examiner's argument continues that, because the prior art works without flaws, Applicant therefore must prove the defects of the prior art with references. Applicant submits that this burden is completely incorrect and inappropriate.

Nevertheless, Applicant has provided references, from peer-reviewed scientific journals, demonstrating that prior art devices cause significant complications. Applicant has further provided details of his own experience as a board-certified ophthalmalic surgeon with thousands of procedures under his belt, concluding that prior art devices cause complications and reduced outcomes. The Examiner rejects this evidence without support. The Examiner did not cite a single reference which supports his arguments. The Examiner produces no affidavit demonstrating that he would have superior knowledge in the field. The Examiner simply rejects the evidence.

The burden lies with the Examiner to demonstrate a *prima facie* case of obviousness, meaning that some combination of prior art references discloses the claimed elements. No such combination exists. Applicant has more than met the burden of demonstrating non-obviousness - a burden that is not Applicant's to meet in the first place. Unless the Examiner produces evidence of record that demonstrates that annular vacuum rings work exactly the same as Applicant's claimed invention, or that porous membranes backed by annular vacuum chambers work exactly as Applicant's claimed invention, and without any flaws, then the rejections must be withdrawn.

THE REFERENCES

The Examiner relies on L'Esperance and/or Hellenkamp as a basis for

every rejection under § 103(a). *OA 07112008 at pp.9-11.* The Examiner acknowledges that neither L'Esperance nor Hellenkamp teach the use of criss-crossing vacuum channels, which is an element of all claims. *OA 07112008 at p. 9.*

L'Esperance. L'Esperance discloses an apparatus for modulating an laser beam applied to an eye lens to ablate the surface for altering the lens curvature, including an eye fixation apparatus with a vertical vacuum annulus 10 over a porous membrane 11 which is in contact with the corneal surface. *L'Esperance, Fig. 1, and col. 4, ll. 26-37.* The porous membrane 11 is subject to clogging by mucous from the corneal surface. *First Will Affidavit, ¶ 9* ("Based on my experience the pores of the L'Esperance design are quite vulnerable to clogging - as is the case with any porous membrane applied to mucus surfaces."); *Second Will Affidavit, ¶ 13.* ("Among other things, it is my professional opinion that the porous membrane with vacuum on one side and mucus on the other would be subject to frequent clogging and be difficult or impossible to properly clean and sterilize.")

L'Esperance does not teach adjustment arms connected to an eye fixation device. L'Esperance does not teach X and Y translation guide members or corresponding translation rods. L'Esperance does not teach the use of docking screws. L'Esperance does not teach shutting off vacuum,

recentering the eye fixation portion, and reapplying vacuum pressure. L'Esperance does not teach a low-profile eye fixation portion so as to fit under the eye lid of a patient.

Hellenkamp. Hellenkamp teaches an eye fixation apparatus using a conventional annular vacuum ring, with "suction enhancement assembly 40" inserted into the vacuum ring to prevent occlusion of the vacuum port. *Hellenkamp, Fig. 4, #40, and col. 7, ll. 59-67.* The suction enhancement assembly includes vacuum ports 55 distributed along insert 40. When vacuum is applied through vacuum port 32, the sclera is displaced into the vacuum annulus defined by 26, 27, and 42, until the sclera is drawn against insert 40. *Hellenkamp col. 5, ll. 1-5; col. 8, ll. 54-60; Fig. 4.* The sclera is not prevented from displacing into the vacuum annulus, but merely from being drawn in far enough to block vacuum port 32. No change to the profile of the conventional vacuum ring is taught by Hellencamp - rather it is a conventional annular vacuum ring. Compare Hellenkamp Figs. 1 and 2, labeled "Prior Art", to Hellenkamp Figs. 4 and 5. A lower profile would actually be incompatible with the insert 40, as the vacuum annulus must have sufficient volume to receive the insert 40 and still provide an unfettered annulus volume 42 above insert 40. *Hellenkamp, Fig. 4, #40, and col. 7, ll. 59-67.* Hellenkamp teaches that the eyeball will bulge upwards into aperture

25 due to the induced distortion. "Specifically, as the suction force is applied to the assembly, the inter-ocular pressure within the eye bulges so as to urge the eye upwardly and into the positioning segment 20." *Hellenkamp, col. 8, ll. 58-61.*

Hellenkamp does not teach criss-cross vacuum channels. Hellenkamp does not teach adjustment arms connected to an eye fixation device. Hellenkamp does not teach X and Y translation guide members or corresponding translation rods. Hellenkamp does not teach the use of docking screws within an eye fixation device. Hellenkamp does not teach shutting off vacuum, recentering the eye fixation portion, and reapplying vacuum pressure, and actually precludes such a method, as discussed below. Hellenkamp does not teach a low-profile eye fixation portion so as to fit under the eye lid of a patient.

Curtin. The Examiner relied on Curtin in combination with L'Eperance or Hellenkamp, and further in combination with Clark and Olson. *OA 07112008 at pp.10-11.* Curtin teaches a conventional annular vacuum ring, essentially the same as Hellenkamp, as part of a grinder apparatus which reshapes the cornea by grinding away corneal tissue. *Curtin, col. 5, ll. 46-51* ("It includes a circumcorneal suction ring 122 which is a conventional device known in opthalmic practice. This device includes

an annular, hollow ring 124 which has an open bottom side which is applied to the surface of the eyeball around the cornea.") Curtin does not teach an adjustment arm, but rather teaches an eye fixation apparatus locked to a base unit which cannot be moved independently. *Curtin Fig. 1, #122, 128.* In Curtin, the "arm" referred to by the Examiner 128 (*OA 07112008 at p.11*) is fixed at its base, which also fixes the eye fixation portion - i.e. the vacuum ring - in space. Minor adjustments may be made, but essentially the eyeball must be adjusted to the vacuum ring rather than adjusting the vacuum ring to the patient's eyeball. *See Curtin, Fig. 2.*

Curtin does not teach the use of criss-cross channels, nor any other eye fixation device beyond a "conventional" annular vacuum ring. Curtin does not teach X and Y translation guide members adjustably connected to an eye fixation portion, nor translation rods to adjust translation guide members. Curtin does not teach the use of docking screws within an eye fixation device. Curtin does not teach shutting off vacuum, recentering the eye fixation portion, and reapplying vacuum pressure. Curtin does not teach a low-profile eye fixation portion which fits under the eye lid of a patient.

Clark et al. Clark teaches apparatus and methods to calibrate the blade extension of a keratome instrument. *Clark, Abstract.* Clark discusses X and Y adjustment only in the context of the disclosed calibration

apparatus, referring to Figs. 1-3 (*Clark, col.4, starting at line 23*). Clark teaches the use of a specialized base platform (*Clark, Fig. 1, #14 "fixture"*) and a "magnifying element" 16 (i.e. a microscope). Fixture 14 is moved to a reference point, then adjusted along an x-axis and a y-axis with the resulting measured displacement providing precise actual calibration measurements of the keratome instrument blade depth. *Clark, col. 7, ll. 4-54.* The X and Y translation is performed away from the patient, away from any eye fixation apparatus, and the apparatus cannot be used to adjust the position of an annular translation member on an eye fixation portion for surgery. *Id.*

Clark does not teach the use of criss-cross channels, nor any other eye fixation device beyond a "conventional" annular vacuum ring. Clark does not teach adjustment arms attached to an eye fixation portion. Clark does not teach the use of docking screws within an eye fixation device. Clark does not teach shutting off vacuum, recentering the eye fixation portion, and reapplying vacuum pressure. Clark does not teach a low-profile eye fixation portion which fits under the eye lid of a patient.

Olson et al. Olson teaches a device for transplanting a cornea. *Olson, Title & Abstract.* The device includes an eye fixation portion consisting of a conventional annular vacuum ring, or "suction ring", arrangement. *Olson, Fig. 1, #3, and col. 1, ll. 57-61.* Olson does teach the

use of set screws to clamp surgical devices.

Olson does not teach the use of criss-cross channels, nor any other eye fixation device beyond a "conventional" annular vacuum ring. Olson does not teach X and Y translation guides or corresponding guide rods. Olson does not teach adjustment arms attached to an eye fixation portion. Olson does not teach discontinuing suction, repositioning the eye fixation apparatus, and re-applying suction.

A. <u>The Section 103(a) Rejection of Claims 1 and 11 over L'Esperance or Hellenkamp</u>

The Examiner rejected Claims 1 and 11 as unpatentable over L'Esperance or Hellenkamp. None of the references cited by the Examiner teach, suggest, or disclose in any way the use of criss-crossing channels for an eye-fixation apparatus. The Examiner has not even presented a *prima facie* case of obviousness. Nor has the Examiner cited any basis for the conclusion that a person of ordinary skill in the art would seek to modify the cited references to eliminate the vacuum annulus designs of the references, other than to argue that the prior art works just as well as Applicant's invention. This is in spite of the Affidavit of Dr. Will providing detailed recitations of the problems caused by prior art devices such as those described by L'Esperance and Hellenkamp, as well as the numerous peer

reviewed scientific papers demonstrating that prior art devices using annular vacuum rings cause complications due, at least in part to scleral displacement. The Examiner provides nothing to bridge the critical gap between the use of a hollow vacuum annulus and the use of criss-crossing vacuum channels other than simply disbelieving Dr. Will's extensive affidavit and other evidence addressing the differences between the claims and the cited references. The Examiner provides no evidentiary bases to refute the evidence submitted by Applicant.

Claims 1 and 11 include the express structural and functional limitation of criss-crossing vacuum channels. All the limitations of a claim must be considered when weighing the differences between the claimed invention and the prior art in determining the obviousness of a process or method claim. MPEP 2116.01; MPEP § 2143.03. Interpreting the claimed invention as a whole requires consideration of all claim limitations. MPEP 2116.01 To establish *prima facie* obviousness of a claimed invention, all the claim limitations as a whole must be obvious to a person of ordinary skill in the art. "All words in a claim must be considered in judging the patentability of that claim against the prior art." MPEP 2143.03 (quoting In re Wilson, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970)). Functional limitations must be given patentable weight, even if it is only

these limitations which distinguish over prior art. DONNER at 479; In re Land, 368 F.2d 866, 151 USPQ 621 (C.C.P.A. 1966); In re Ludtke, 441 F.2d 660, 169 USPQ 563, 566 (C.C.P.A. 1971); In re Atwood, 354 F.2d 365, 148 USPQ 203, 210 (C.C.P.A. 1966).

The references L'Esperance and Hellenkamp do not disclose the combinations of elements recited in independent Claims 1, 11 and 12, nor has any reference been asserted teaching or suggesting such modification, and therefore the Examiner has not established a *prima facie* case of obviousness. None of the references discloses apparatus or methods for an eye fixation apparatus utilizing *criss-crossing channels* on a convex bottom contact portion, without use of a vacuum annulus over the contact portion, nor do they disclose apparatus or methods capable of repositioning a vacuum-based eye fixation apparatus after vacuum has been applied initially. In fact, none of the references cited by the Examiner disclose use of criss-cross channels at all. The use of criss-cross channels distinguishes claims 1, 11, 22 and 12/11 over the Examiner's cited references.

The Examiner provides no basis for disputing Applicant's description of the cited references' weaknesses, other than to argue that the prior art patents are "presumed valid" so Applicant's invention cannot be an unobvious advance. Applicant has never argued that the Examiner's

references are invalid, merely that they do not address or solve the problems solved by Applicant's inventions. Reference to Dr. Will's affidavits provides explanation of the unique features of the present invention, and the significant differences from the prior art cited by the Examiner. Nowhere does the Examiner cite any reference upon which to base his conclusory statements that Dr. Will is incorrect, or that prior art devices work so well that no subsequent improvements in the art are possible.

L'Esperance discloses a method and apparatus for modulating the flux distribution onto a surface to be profiled of an ablative radiation beam, including a fixation device which uses a porous membrane backed by a hollow vacuum chamber annulus. *See L'Esperance, Fig. 1 and col. 4, ll. 28-34* (describing "a hollow annulus.") L'Esperance does not focus on the fixation apparatus but rather on the laser ablation apparatus and methods, especially lensing methods. The description of the fixation means is simply a "hollow annulus, having a convergent axial end wall 11 of air-permeable material contoured to engage and retain an eye via a scleral-corneal region." *L'Esperance col. 4, ll. 25-35.*

L'Esperance does not disclose using criss-cross channels for distributing vacuum, nor any means for fixation not requiring "a hollow annulus." L'Esperance does not even address the problems of scleral

damage caused by vacuum fixation devices. Therefore, L'Esperance does not render Applicant's solution obvious.

The Hellenkamp reference, cited by the Examiner, specifically discusses the problem of mucus accumulation which can occlude vacuum components, during procedures and after hardening, and which requires special cleaning procedures to remove. *First Will Aff. ¶ 5.h; Second Will Aff. ¶ 13.* The removable vacuum member in Hellenkamp is specifically intended as an attempt to address this problem, among others, but it is an incomplete solution at best. *See Hellenkamp, col. 5, ll. 43-5.* The Examiner states, "Applicant then states the 'criss-cross channels, providing alternating lands grooves, are fundamental to the present invention', however, there has been no showing of the criticality of this particular arrangement of voids and barriers." *OA 04112007 at p.10.* Applicant submits that this is the focus of much of the application itself – it is one of the stated advantages over existing devices. Moreover, Dr. Will's affidavits discuss the differences, and resulting advantages, of his criss-cross channels over existing devices such as L'Esperance and Hellenkamp in detail. The language the Examiner cites states merely that the particular orientation of the criss-cross channel intersections is not limited to the preferred embodiment.

The Examiner's definition of a porous membrane as simply

comprising alternating lands and grooves is unsupportable. *OA 04112007 p. 10-11.* A porous membrane requires flow paths from the contact surface through the membrane and open to the back-side surface. It *requires* a *permeable* membrane. A permeable membrane is not in any manner the same as alternating lands and grooves created by a criss-cross vacuum channel. The Examiner needs to cite some objective source for this claimed equivalence and cannot simply declare it so.

The Examiner referenced an article by Benitez-del-Castillo et al, *Decrease in Tear Secretion and Corneal Sensitivity After Laser In Situ Keratomieusis*, CORNEA, vol. 20(1), January 2001 at pp. 30-32 (*OA 06142007 at pp. 7-8*). The reference, a copy of which was provided by the Examiner and is included in the Evidence Appendix, does not profess to answer the causes of dry eye complications after LASIK, it merely confirms that such complications do indeed occur. Applicant's invention, as explained in the Specification, seeks to address some of the causes of complications and less than optimal outcomes. The Examiner's article reference does not obviate the different approach that Applicant has taken to solve these problems.

Hellenkamp discloses an eye fixation apparatus utilizing an annular hollow vacuum ring with a vacuum ring insert to prevent complete occlusion

of vacuum caused by chemosis or buildup of mucous in the vacuum ring. The vacuum ring insert simply is intended to prevent complete occlusion, not prevent damage such as chemosis. *Hellenkamp col. 5 ll. 25-30* ("to maintain the suction channel evacuated even in the presence of chemosis"). Thus Hellenkamp does not solve the problem of chemosis and damage, it merely attempts to deal with the problem as it relates to loss of vacuum. Hellenkamp, however, acknowledges that damage does occur from the operation of annular vacuum rings.

The Examiner states, "Both L'Esperance (EP '127) and Hellenkamp teach a device and method as claimed except for the criss-cross passages." *OA 06142006 p.5*. The criss-cross channels, providing alternating lands and grooves, are fundamental to the present invention, and are not disclosed by the cited references. L'Esperance and Hellenkamp do not disclose means for fixing an eye for surgery other than a hollow annulus. A hollow annulus has specific disadvantages not appreciated by either L'Esperance nor Hellenkamp which are addressed by the present invention, as pointed out by the accompanying Affidavit of Dr. Will. Several journal articles discussing complications caused by use of vacuum rings such as taught in Hellenkamp, Curtin and Clark, are addressed in the *Second Aff. Will, ¶¶ 6-11 and Exh. 1-6*. The articles were provided to the Examiner to address the Examiner's

skepticism that prior art devices caused complications in surgery. The articles demonstrate that the problems which Applicant seeks to address are real world problems, and not mere "speculation" as asserted by the Examiner (without basis). *OA 04112007 p. 8.*

The Examiner's rejections appear to be based on a view that the Applicant is required to prove that the references cited by the Examiner are non-functioning, or that such references must be presumed full proof and without significant drawbacks, in order to claim an invention with improved results over the existing art. The burden lies with the Examiner to demonstrate that Applicant's invention is obvious through citation to record evidence rather than simply relying on conclusory statements that he is "unconvinced." The Examiner states that because L'Esperance and other references are patents they are "presumed valid" and therefore L'Esperance's porous membrane does not clog. *OA 06142007 at p.8.* Applicant submits that the Examiner misapprehends the difference between patent validity and perfection. The mere fact that a patent is presumed valid does not imply that such a patent solves, perfectly and forever more, all problems associated with the field of art such that no new patentable device may ever issue in the future.

Needless to say, there is likely more than one cause of "dry eye" after

LASIK, and Dr. Will is not required to disprove the Examiner's thesis in order to establish that his invention reduces potential for this complication, and that a potential source of the complication is damaged sclera caused by conventional vacuum rings. A copy of the Albietz reference cited in the *First Will Aff., ¶ 8, and Second Will Aff. ¶ 10 and Exhibit 5,* is provided with this Brief in the Evidence Appendix. The purpose of the reference is to demonstrate that problems do exist with existing annular vacuum ring designs such as Hellenkamp.

The difficulty in cleaning is discussed as a general hindrance which can reduce the patient turnover rate. *See Hellenkamp, col. 3, l. 45 – col. 4, l. 12.* The same difficulties with clogging and effective cleaning described in Hellenkamp are magnified in a porous membrane as taught by L'Esperance. Additional drawbacks include higher risk of patient cross-contamination with viral, bacterial and prion material. *First Will Aff. ¶ 5.h.* The present invention provides a relatively smooth and impermeable surface with shallow cross-connected channels which are easily cleaned using conventional methods, thereby extending the life of the apparatus. The cross-connection prevents loss of vacuum from occlusion of any single channel due to buildup.

Additionally, the hollow annulus designs inherent to L'Esperance and

Hellenkamp require the use of a lid speculum on patients with narrow ocular orbits. *First Will Aff.* ¶¶ *7-8; Second Will Aff.* ¶¶ *15-17* . The use of lid specula causes undesired negative side effects which have been documented, and are an ever increasing problem as procedures such as LASIK become more widespread. Dr. Will's Affidavit specifically addresses the complications caused by conventional hollow annulus apparatus. The use of criss-cross channels with alternating lands and grooves in the present invention avoids the need for lid speculum even in patients with narrow orbits because it allows a lower profile device. Examiner failed to point to any reference which teaches criss-cross vacuum channels, creating a low profile apparatus which can fit underneath the eyelids, obviating the need for a lid speculum during surgery. All of the art cited by the Examiner relies upon an annular design necessitating a vault, with the exception of Ruiz, which does not teach the use of a vacuum fixation apparatus at all and so does not support a rejection.

The use of criss-cross channels minimizes distortion of the eye lens which causes less than optimal correction to patients' vision. The criss-cross channels prevent or minimize damage to the cornea, sclera and conjunctiva which has been a documented problem in LASIK and other keratome procedures using apparatus such as relied upon by the Examiner. The criss-

cross channels permit a low-profile device which can fit under patients' eye lids, obviating the need for a lid speculum, thereby reducing complications in patient recovery and reducing obstructions during surgery. These complications are especially relevant for patients with narrow ocular orbits. Dr. Will's Affidavit also provides citation to references which provide objective evidence to back up his explanations of the differences and advantages of his invention over the prior art demonstrating the nonobviousness of the claims. *First Will Aff. ¶¶ 7-8.*

The Examiner incorrectly states that there is no disclosure in the Application relating to holding the corneal surface flat, without displacement into the criss-cross vacuum channels. *OA 07142006 at p. 3.* The original specification at page 6, lines 12-20, states:

> "When placed on the eye, with the contact portion **14** contacting directly upon the eye and encircling the cornea, the criss-crossing channels **16** are upon the eye globe conjunctiva. Vacuum port **18** communicates with channels **16** such that vacuum pressure exerted at the vacuum port **18** creates vacuum pressure in the criss-crossing channels **16**, *sucking the eye globe conjunctiva attached to the sclera flush against the contact portion **14**.* This fixates the eye. The criss-crossing channels **16** work to oppose the suction created by each other, such that *the eye glove conjunctiva attached to the sclera, is spread taut between the channels **16**, instead of being sucked upon into a particular channel.*"

Specification, page 6, lines 12-20 (emphasis added). Further, the Specification's "Summary of the Invention", at page 4, lines 11-21, recites

decreased trauma to the ocular surface and the ability to more easily reposition the fixation device after vacuum has once been applied as specific advantages of the present invention. Further, Dr. Will's accompanying Affidavit for further evidence in this regard. In contrast, the Hellenkamp reference relied on by the Examiner specifically acknowledges that the cornea is displaced into the hollow vacuum ring to contact the surface of the vacuum enhancer. *Hellenkamp at col.9, ll. 23-43.* Conversely, the Examiner provided no record evidence to support his incorrect factual assertion that the present invention does not draw the cornea surface to contact against the flat land between the criss-cross channels, rather than into the channels themselves, as claimed and described.

Additionally, the use of criss-cross channels (a recited element of each claim) avoids the problem of clogging which porous surfaces (such as taught in L'Esperance) are subject to. The use of channels also permits a lower profile than devices using a porous surface can achieve because there is no need for the vacuum annulus above the porous surface (as taught in L'Esperance). Thus, the present invention provides unobvious solutions to the problems inherent in existing apparatus and methods.

Although specific vacuum pressures are not claimed, the ability to use lower vacuum pressure for eye fixation is an advantage of the criss-cross

vacuum channel design over prior art structures which is evidence supporting the non-obvious differences over the structures disclosed in the cited references.

The Affidavit of Dr. Will directly addresses the inherent problems with existing devices and methods and the specific structures and methods which solve these problems. *First Will Aff. ¶¶ 5-9; Second Will Aff. ¶¶ 6-15.* The references submitted with the Second Will Aff. discuss complications from current LASIK and other ophthalmological surgical procedures, and indicate that the use of vacuum rings may be a significant, though certainly not the only, cause. *Second Will Aff. ¶¶ 6-15, Exhibits 1-6.* Applicant has made clear that a significant disadvantage of existing designs such as Hellenkamp, Curtin, and others is that they rely on a hollow annular ring to apply vacuum, which causes the cornea surface to displace into the vault of the ring. The vacuum enhancer taught by Hellenkamp reduces this problem in certain respects, but does not eliminate it. Applicant has also explained that the vault – inherent in the design of existing hollow annular rings, including Hellenkamp, Curtin and L'Esperance – creates the need for a lid speculum during procedures, which is generally eliminated by the low profile of the criss-cross channel design which is recited in all claims of the present invention. Applicant, by pointing out these specific drawbacks of

existing apparatus and methods, does not argue that these references are inoperative or invalid, but merely that they are not perfect solutions. The present invention represents a significant improvement over existing apparatus and methods in many respects, discussed in detail in Dr. Will's Affidavit. The Examiner incorrectly implies that by claiming improvement over the existing art Applicant must prove the existing art lacks utility.

Pores are not lands and grooves.

The Examiner describes the pores of L'Esperance as lands and grooves but cites no support for this. *OA 06142007 at pp. 10-11.* A porous surface would necessarily be considered smooth, lacking lands and grooves. Referring to L'Esperance's porous surface as lands and grooves extrapolates the minimal teachings of L'Esperance much too far. L'Esperance teaches a porous, air-permeable membrane. This is not equivalent to criss-crossing channels creating lands and grooves. L'Esperance applies suction through a porous membrane via an annular chamber above the porous membrane. *See L'Esperance '127 at col.4, ll.26-34.* This is the only method taught by L'Esperance '127 and its related applications.

The Examiner correctly notes that the porous surface of L'Esperance distributes vacuum over its surface to improve stability. However, such porous surfaces are subject to clogging. All porous materials are subject to

clogging if mucous is sucked through them, a simple fact of nature. Examiner cited nothing in L'Esperance or any other reference suggesting special properties which render L'Esperance's porous membrane not subject to clogging. Rather than placing the burden on Applicant to find a reference describing L'Esperance's shortcomings, the burden rests with the Examiner to cite a reference explaining how Dr. Will's description of L'Esperance's tendency to clog is not correct. The fact that L'Esperance does not address this problem does not render it inapplicable – L'Esperance was primarily focused on issues unrelated to the eye fixation methods. Hellenkamp addresses significant problems with buildup of mucous and other debris within vacuum channels leading to occlusion. The Examiner fails to explain how the pores of L'Esperance are free of clogging issues whereas the full bore annular vacuum rings of Hellenkamp are subject to occlusion. Dr. Will stated in his affidavit that based on his actual experience conducting surgeries that the porous membrane of L'Esperance would be subject to clogging. *First Will Aff.* ¶ *9.*

The Examiner states, "It is not clear to the examiner why" a low profile device obviates the need for a lid speculum. *OA 06142007 at p. 6.* Applicant addressed this question in the *Second Will Aff.* ¶ *14-16* . Devices relying on a vaulted vacuum annulus, such as L'Esperance and Hellenkamp,

require use of a lid speculum. *Id.* Dr. Will has performed thousands of eye surgeries. Respectfully, Applicant submits that if the Examiner disputes facts in Dr. Will's affidavit then the burden rests on the Examiner to prove his contentions based on references which can be made part of the record, so that Applicant may respond and reviewing bodies can review the evidence. Moreover, Dr. Will stated that based on his direct experience, that of his staff, and his research, existing devices operating similar to L'Esperance and Hellenkamp face limitations which the present invention addresses. *Second Will Aff.* ¶¶ 2-4. Applicant submits that the Examiner failed to cite reliable references in the record.

The Examiner states that L'Esperance's membrane forms only "a portion" of the device but extends beyond the annular chamber and so would fit under the eye lid. *OA 06142007 at p. 7.* Applicant points out that this extending lip does not convey vacuum as there is no vacuum source above it. A membrane would conduct vacuum only through its plane, not laterally. Thus the annular chamber necessarily is concurrent in area with the vacuum-affected surface of the membrane. The annular access provided for surgical access is inside the inner diameter of the vacuum annulus. By contrast, as pointed out in Dr. Will's affidavits and the Specification and Drawings, the criss-crossing channels extend from the annulus provided for surgical access

outward, with no vacuum annulus above them. The criss-cross channels therefore provide an inherently lower profile. Again, neither L'Esperance nor Applicant's figures are drawn to scale so the Examiner's attempts to measure proportions is inappropriate. One can observe the structures and note that there is indeed, necessarily, a vacuum annulus extending vertically above the membrane of L'Esperance (*see Fig. 1, #10, 11, 12 & col. col. 4 ll. 28-35*), while the vacuum channels of claims 1, 11 and 22 extend laterally with no vertical vacuum annulus rising above, allowing a narrow profile for an eyelid to fit over (see Fig. 4).

The Examiner equates the vacuum distributor inside the suction ring of Hellenkamp equates to the distributed lands and grooves created by the criss-crossing channels of claims 1, 11 and 22. *OA 06142007 at p. 5.* The problem with the Examiner's evaluation is that in Hellenkamp the sclera does not contact the surface of the insert *until it has been sucked into the annulus of the vacuum ring* – thus substantially all of the damage has already been done. Nowhere does Hellenkamp teach, nor do the drawings of Hellenkamp illustrate, a flush-mounted land and groove contact surface. Hellenkamp never contemplated a solution involving anything other than a vacuum ring. Moreover, Hellenkamp merely attempts to distribute vacuum more evenly – but this is only a partial solution. The real damage is caused

by displacement into the vacuum ring itself, which Hellenkamp does not prevent. L'Esperance, while able to prevent displacement has the potential of causing the opposite problem. If the pores of L'Esperance clog then either of two outcomes is likely. Either vacuum hold will be lost, allowing the fixation apparatus to move or separate completely from the cornea, or, the clogged pores will lock the vacuum between the membrane surface and the conjunctiva with no way to break the vacuum. The result is that the apparatus must be separated under vacuum potentially tearing the sclera. Either outcome is undesirable. The criss-cross channels of Applicant's invention prevent displacement into a annular vacuum ring without the danger of clogging created by L'Esperance's membrane.

The lands of the criss-crossing channels provide the contact surface without being drawn into an annular ring. The vacuum channels are on opposing sides of any given land such that they act against one another to pull the sclera against the lands between rather than displacing into the channels themselves.

The prior art teaches away from non-use of lid specula and lowering IOP.

Both Hellenkamp and L'Esperance teach vacuum rings with annular vaults requiring the use of lid specula causing greater discomfort for

patients. *See First Will Aff. at ¶ 8.* L'Esperance '172 (cited by the Examiner), which is a continuation-in-part of Application 891,285 issued as L'Esperance '148 (also cited by the Examiner), specifically teaches the requirement of using a lid speculum and can therefore be viewed as teaching away from apparatus and methods which do not require such. *See L'Esperance '172, col.3, ll.50-59.* "A prior art reference may be considered to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant." Monarch Knitting Machinery Corp. v. Sulzer Morat GmbH, 45 USPQ2d 1977 (Fed. Cir. 1998). *See also* The Dow Chemical Co. v. U.S.,18 USPQ2d 1657 (Ct. Cl. 1990). The use of criss-crossed channels with alternating lands and grooves, a recited element in all claims of the present invention, eliminates the need for annular vaults thereby creating a lower profile device. This lower profile eliminates the need for a lid speculum in most cases, and is more comfortable for patients, especially those with narrow or tight lid openings. This fundamentally distinguishes the present claims from L'Esperance.

The use of the criss-cross channel design also reduces deformation with the goal of fixating the eye while minimizing raising IOP. This is in

direct contrast to the teachings of the prior art which teach increased IOP as desirable. *Hellenkamp col. 8, ll. 54-64; Second Will Aff. ¶ 18 and Exh. 1-6.*

The Examiner must provide an affidavit to rely upon personal knowledge.

Applicant does not argue that the prior art cited lacks utility or is non-functional, but the present invention provides unobvious improvements over the cited references which achieve greater accuracy and less discomfort from patients, while making laser keratome procedures more economical for practitioners.

Further, if the Examiner relies on personal knowledge to assert that:

(1) L'Esperance and Hellenkamp are not subject to clogging or occlusion;

(2) neither L'Esperance nor Hellenkamp cause damage to the cornea/conjunctiva surface when vacuum is applied and removed; and,

(3) that use of high profile hollow annular rings as taught by the Examiner's cited references does not cause complications and discomfort to patients;

then the Examiner is required to provide an affidavit explaining the basis of such knowledge. *See* MPEP 2144.03(A) [R-1] ("It is never appropriate to

rely solely on "common knowledge" in the art without evidentiary support in the record, as the principal evidence upon which a rejection was based.: (omitting citations)). Further, "While 'official notice' may be relied on, these circumstances should be rare when an application is under final rejection..." MPEP 2144.03(A) [R-1].

> "It would not be appropriate for the examiner to take official notice of facts without citing a prior art reference where the facts asserted to be well known are not capable of instant and unquestionable demonstration as being well-known. For example, assertions of technical facts in the areas of esoteric technology or specific knowledge of the prior art must always be supported by citation to some reference work recognized as standard in the pertinent art. *In re Ahlert*, 424 F.2d at 1091, 165 USPQ at 420-21. See also *In re Grose*, 592 F.2d 1161, 1167-68, 201 USPQ 57, 63 (CCPA 1979)"

MPEP 2144.03(A) (emphasis original). "If the examiner is relying on personal knowledge to support the finding of what is known in the art, the examiner must provide an affidavit or declaration setting forth specific factual statements and explanation to support the finding. *See* 37 C.F.R. 1.104(d)(2)." MPEP 2144.03(C) [R-1] (emphasis added). Furthermore, Section 103 requires analysis of a claimed invention as a whole:

> "Focusing on the obviousness of substitutions and differences, instead of on the invention as a whole, is a legally improper way to simplify the often difficult determination of obviousness."

Gillette Co. v. S.C. Johnson & Son Inc., 16 USPQ2d 1923 (Fed. Cir. 1990).

B. The Rejection of Claim 12 over L'Esperance or Hellenkamp

Applicant reiterates the arguments in Section A, above.

The Examiner also asserts that "to discontinue vacuum and reposition the apparatus if it is not centered on the cornea [is obvious], since proper positioning of the corneal flap is critical..." *OA July 14, 2006, at p. 5.* This simply misses the point. The apparatus and methods of the references cited by the Examiner actually *prevent* discontinuation of vacuum and repositioning of the apparatus due to the negative effects of using a hollow annulus to apply vacuum, as explained by the First and Second Will Affidavits. All of the discussion relating to the damage created by vacuum rings caused by scleral displacement into the vacuum ring chamber have been addressed above. The damage caused by vacuum rings prevents repositioning after application of vacuum. *First Will Aff.* ¶ *5.*. L'Esperance is subject to clogging which can cause the apparatus to adhere to the sclera even after vacuum pressure is removed. *First Will Aff.* ¶ *9.a.* These dangers are alleviated by the method recited in claim 12/11 - the use of criss-cross channels avoids the "hickey" effect and prevents post-vacuum adherence. Thus, the Examiner's arguments regarding obviousness actually demonstrate the nonobviousness of using a system of criss-cross channels providing alternating lands and grooves. In addition, L'Esperance and Hellenkamp

retain the significant disadvantage that they require lid speculum during most procedures (due to the inherently high profile of the hollow annulus), especially for patients with narrow ocular orbits, and they contain no teachings to indicate a solution. Other disadvantages of the L'Esperance and Hellenkamp references, which are addressed by the present invention, are made apparent by the accompanying Affidavit of Dr. Will.

The Examiner states that both L'Esperance and Hellenkamp teach the device as claimed "except for the criss-cross passages" and use of such channels is obvious because "this is another configuration that would serve to distribute vacuum and thus provides no unexpected results." *OA 07112008 p. 9.* The Examiner went on to say that to "discontinue the vacuum and reposition the apparatus" is also obvious. This is clear hindsight analysis, and requires the Examiner to completely disregard the Applicant's affidavits, as well as the entire Specification and Claims. Applicant explained, in detail, based upon years of experience and thousands of procedures, and a thorough knowledge of prior art devices, that apparatus using the annular vacuum rings of Hellenkamp or the annular chamber and porous membrane of L'Esperance, prevent the discontinuance of vacuum and repositioning of the fixation apparatus. The references cited therefore do not render such a method obvious, as they preclude such a method. The

Examiner simply discounts the Applicants submission without citation to any reference nor any affidavit by the Examiner. The Examiner must produce evidence of record.

C. <u>The Rejection of Claims 2 and 13 over L'Esperance or Hellenkamp in combination with Curtin.</u>

Applicant reiterates the arguments in Sections A & B, above.

Dependent Claims 2 and 13 were rejected under § 103(a) as unpatentable over L'Esperance or Hellenkamp in combination with Curtin. Traversal with respect to L'Esperance or Hellenkamp is reasserted regarding independent claims 1, 11 and 12 and further with regard to their combination with Curtin, which teaches a conventional hollow annular ring. *Curtin, col.5, ll. 46-51.*

The Examiner asserts that "Curtin teaches the use of adjustment arms on eye fixation devices." *OA 07112008 at p.10.* Applicant respectfully disagrees. Curtin specifically teaches that the rigid vacuum tube 128 holds annular ring 124 stationary over an eyeball, at which point the patient is provided a target to focus on which aligns the eye to the apparatus. Vacuum is applied to annular ring 124 which then "locks the ring arrangement 122 on the patient's eye when the patient's visual axis is aligned with the target." *Curtin, col.6, ll. 1-8; col. 7, ll. 29-39 & 63-68.* Curtin does not, alone nor in

combination with other references cited, teach or suggest the use of adjustment arms connected to an eye fixation apparatus which permit adjustment of the apparatus to the eyeball prior to fixation, rather than having the eyeball align itself to a vacuum ring. Thus Curtin teaches exactly the opposite methodology of the current invention recited in claims 2, 13 and 22, which renders it less optimal than the current invention.

Dr. Will, in his affidavit, notes several advantages from the use of adjustment arms. *See First Will Aff. ¶ 10.c.* Maneuvering the device is easier, and there is less chance that inadvertent contact will scratch the conjunctival surface or cause contamination. While the single adjustment arm of Curtin may have 3-D adjustment capability as argued by the Examiner, such capability does not equate to the ease of use provided by the arms of the present invention which would allow a surgeon to grip the arms with each hand while sighting through the annular access hole with a sighting device, rather than the cumbersome apparatus described in Curtin. A person of skill in the art would not see the combination of Curtin with L'Esperance and/or Hellenkamp as teaching the combination of elements of claims 2 and 13.

D. The Rejection of Claims 3, 4, 7, 8, 14, 15, 18 and 19 over L'Esperance or Hellenkamp in combination with Curtin and Clark.

Applicant reiterates the arguments in Sections A through C, above.

Dependent Claims 3, 4, 7, 8, 14, 15, 18 and 19 were rejected under § 103(a) as unpatentable over L'Esperance or Hellenkamp in combination with Curtin and/or Clark et al.

The Examiner incorrectly states that "Clark et al teach employing X- and Y- axis adjustment mechanisms on eye fixation devices." *OA 07142007 at p.15.* Applicant respectfully disagrees. Applicant has not claimed the concept of X-Y adjustment, but a particular apparatus and method of lateral and cross-lateral position adjustment integrated into an eye fixation portion for use during surgical procedures.

As makes clear in the *First Will Aff.*, the ability to adjust the fixation apparatus to the eyeball, rather than vice versa, provides for better adjustment and concentration properties during laser procedures. This adjustment capability is enhanced by the addition of lateral translation members directly to the eye fixation apparatus. Translation guide rods with knob adjusters allow precise adjustments while requiring less manual dexterity than current apparatus and methods. The translation guide rods

also prevent further distortion of the eyeball caused by forcing the eyeball into alignment with the surgical apparatus.

1. Claims 3 and 14 over L'Esperance or Hellenkamp, Curtin and Clark.

The Examiner argues that "Curtin teaches the use of translation rods and adjustment knobs to allow the adjustment in 3 dimensions of an ophthalmic surgical instrument." *OA 07112008 at p.10.* However, the mere ability to move through space does not render obvious a structure including translation guide members connected to an eye fixation apparatus and their methods for use.

Applicant's claims are drawn to *annular* X and Y translation members (Fig. 5, #40, #60) connected to the eye fixation portion (Fig. 5, #12) of an eye fixation apparatus, and methods to use these translation guide members. Curtin teaches an apparatus for moving surgical instruments separate from the fixating vacuum ring rather than connected to it, an apparatus which is not annular in any way. *Curtin Fig. 1, #16, #32.* Nothing in Curtin teaches annular X or Y translation guide members adjustably connected to an eye fixation portion as recited in claims 3, 7, 14 and 18. The "eye fixation portion" (#12) as recited in the claims refers to the lower part of the eye fixation apparatus, the part which actually contacts the patient's eyeball.

Clark discloses a microscope apparatus for bench aligning a microkeratomy blade. Clark The microscope target table includes the ability to move in an X-Y orientation, but the structures do not disclose and do not equate to annular translation guide members connected to an eye fixation device - i.e. on a patient's eye - for surgery. Clark, Fig. 23, discloses a keratome blade device moving across a surface in a single direction, but the kerotome device is not an *annular* translation guide member, and is adjustable only in the vertical direction. The blade of Clark does not disclose the same structure, nor the same function or effect, as the annular translation guide member recited in claims 3 and 14.

2. Claims 7 and 18 over L'Esperance or Hellenkamp, Curtin and Clark.

Applicant reiterates the arguments in Section D.1, above.

Applicant reiterates the arguments above. Curtin does not teach a translation guide member connected to an eye fixation portion. Even if one were to interpret Clark as teaching a translation guide member connected to an eye fixation portion, Clark is silent regarding any additional utility of a second translation guide member.

3. Claims 4, 8, 15 and 19 over L'Esperance or Hellenkamp, Curtin and Clark.

Applicant reiterates the arguments in Sections D.1 through D.2, above.

Additionally, neither Curtin nor Clark teach the use of translation guide rods and adjustment knobs to adjust one or more translation guide members connected to an eye fixation portion as recited in claims 4, 8, 15 and 19.

Applicant acknowledges the Examiner's explanation of how adjustment screws operate, but this does not render the claims obvious. *OA 04112007 at pp. 9-10.* The statement that the Examiner refers to is at *First Will Aff. ¶ 11*, where he refers to the fact that seemingly minor changes in apparatus and methods can actually achieve significant results in surgical procedures where "adjustments in the sub-micron range" can alter outcomes. The reference was to all of the differences over the prior art in the previous ten paragraphs. Thus, the reductions in eye deformity, intraocular pressure variations, reductions in hydration variation of the cornea, improved positioning capabilities, improved re-positioning capabilities, improved adjustment capabilities, and lessened complications achieved by the apparatus and methods claimed, all lead to significantly improved outcomes

individually and cumulatively. The point was that improvements over prior art devices in positioning or focusing LASIK apparatus may, in some cases, only be in the sub-micron range, but even such small *improvements* can be significant.

In addition, Dr. Will's affidavit makes clear the differences between the present invention and the asserted references. X-Y adjustment ability for adjusting surgical apparatus prevents further distortion of the eyeball caused by forcing the eyeball to alignment with the apparatus, rather than vice versa. It also eliminates the need for expensive and complicated software to adjust for laser offset.

4. Claim 16 over L'Esperance or Hellenkamp, Curtin and Clark.

Applicant reiterates the arguments in Sections D.1 through D.3, above.

Additionally, neither Curtin nor Clark disclose a method of using docking screws for tightening against objects within an annular translation guide member. The vacuum ring of Curtin has no means of connecting an annular translation guide member, nor of tightening a docking screw against objects inerted into the vacuum ring. *Curtin, Fig. 1, #124.* Nor does Clark disclose any set screw for tightening against and object within an annular

translation guide member. *Clark, Fig. 23, #37, #39.* Therefore, the Examiner has not established a *prima facie* case of obviousness.

5. The Rejection of Claims 5, 6, 9, 10, 17 and 20-22 over L'Esperance or Hellenkamp and Curtin and Clark, and in addition Olson.

Applicant reiterates the arguments in Sections D.1 through D.4, above.

Dependent Claims 5, 6, 9, 10, 16, 17, 18 and 19 were rejected under § 103(a) as unpatentable over L'Esperance or Hellenkamp and Curtin in combination with Clark et al, and further in regard to U.S. 6,613,061 Olson. Applicant acknowledges that Olson teaches the use of docking screws. Applicant does not claim to have invented docking screws, but the claims as a whole incorporating docking screws are novel and unobvious in combination with annular translation guide members adjustably connected to an eye fixation portion.

None of the cited references, even in combination, teach all the elements of the rejected claims. Applicant reiterates the discussion above, relating to the lack of teaching of first and second annular translation guide members in the cited references. Olson does not teach the use of docking screws to tighten against objects inserted into the cylindrical space formed

by the first (or second) annular translation guide members.

The Examiner's additional reliance on Ruiz does not disclose the elements of the claim either. Ruiz teaches a geared cutting blade on a base which lacks the ability to fix the eye in space, and so still fails to disclose, even in combination, all of the elements of the rejected claims. Ruiz does not disclose use of docking screws to tighten against objects in the annulus, especially considering Ruiz teaches a movable cutting blade. Nor does Ruiz teach the use of a second translation guide member non-parallel to a first translation guide member to permit X-Y adjustments with a docking screw.

Notably, Olson teaches the use of a conventional vacuum ring for eye fixation. *Olson Fig. 1 #4 & 5; col. 1, ll. 55-60.* This is yet another reference teaching the use of vacuum rings, in contrast to the criss-cross channel design of Applicant. The Examiner failed to establish a *prima facie* case of obviousness under Section 103(a).

In addition, Dr. Will's affidavit makes clear the differences between the present invention and the asserted references. X-Y adjustment ability and the use of docking screws for setting and adjusting surgical apparatus prevents further distortion of the eyeball caused by forcing the eyeball to alignment with the apparatus, rather than vice versa. It also eliminates the need for expensive and complicated software to adjust for laser offset. The

claims are unobvious.

E. <u>The Rejection of Claim 22 over L'Esperance or Hellenkamp and Curtin and Clark, and in addition Olson.</u>

Applicant reiterates the arguments in Sections A through D, above.

Independent Claim 22 stands on its own. The Examiner rejected claim 22 under § 103(a) based on a combination of L'Esperance or Hellenkamp in combination with Curtin and Clark et al, and further in combination with Olson. Claim 22 includes all of the structural elements of claims 1-10 but explicitly recites the limitation "wherein the eye fixation portion has a low profile convex bottom contact portion..." and "...is substantially narrow so as to fit under the eye lid of a patient without the use of a lid speculum." Support for claim 22 is found in the Specification at page 4, ll. 11-14 and Fig. 4. The Specification, at page 4, lines 11-14, describes a feature of the invention that "(1) functions without the need for a lid speculum; (a) low profile fits comfortably under the lids; (b) can more easily be used on patients with "tight lids" which are common to some races..."

Applicant reasserts each of the arguments regarding rejections of claims 1-21, above, in regard to Claim 22. None of the cited references, even in combination, discloses all of the elements of claim 22 much less

discloses the combination of the elements. Specifically, the references do not disclose a low profile fixation portion with criss-cross channels, first and second translation guide members with adjustment rods and knobs, docking screws in the first and second translation guide members, wherein the profile of the fixation portion – i.e. the structure containing the vacuum channels – is low enough to fit under the eye lid of a patient to obviate the need for a lid speculum.

F. Method Claims 11-21.

Applicant asserts that method claims 11-21 stand on their own. The Examiner cited no reference or combination of references which recite the steps of method claims 11-21, but has merely cited references which include some, but not all, structural elements of apparatus claims 1-10. Applicant here reasserts all of the arguments relating to apparatus claims 1-10 relating to structural limitations inherent in claims 11-21, and additionally argues that the method steps are not disclosed by any combination of references, nor are they disclosed by any obvious modification of such references. Therefore, even if apparatus claims 1-10 and 22 are held obvious, Applicant submits method claims 11-21 are not thereby rendered obvious and stand on their own.

SUMMARY

For the foregoing reasons, Appellant requests reversal of Examiner's rejections of Claims 1-22.

Respectfully submitted,

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CLAIMS APPENDIX

Listing of Claims:

1. An eye fixation apparatus, comprising:

an eye fixation portion, wherein the eye fixation portion has an annular convex bottom contact portion, said convex bottom contact portion including a concave bottom surface which goes upon the surface of an eyeball and encircles the cornea, and wherein the contact portion bottom surface is provided with criss-crossing channels; and

a vacuum port connected to said eye fixation portion and in communication with said criss-crossing channels such that vacuum pressure applied to said vacuum port exerts vacuum pressure through such criss-crossing channels to pull the eyeball membrane to the criss-crossing channels.

2. The eye fixation apparatus of claim 1, further comprising adjustment arms connected to said eye fixation portion.

3. An eye fixation apparatus of claims 1 or 2, further comprising a first annular translation guide member adjustably connected to the eye fixation portion, wherein the first translation guide member portion can translate laterally in relation to the eye fixation portion.

4. The apparatus of claims 3, wherein the first translation guide member

is provided with a first translation rod and a first adjustment knob for translating the first translation guide member.

5. The apparatus of claims 3, further comprising a docking screw screwed through the first translation guide member for tightening the first translation guide member against objects inserted into the cylindrical space formed by the first annular translation guide member.

6. The apparatus of claims 4, further comprising a docking screw screwed through the first translation guide member for tightening the first translation guide member against objects inserted into the cylindrical space formed by the first annular translation guide member.

7. The apparatus of claims 4, further comprising a second translation guide member adjustably connected to the first translation guide member, wherein the second translation guide member can translate laterally in relation to the first translation guide member in a direction not parallel to the translation of the first translation guide member.

8. The apparatus of claims 7, wherein the second translation guide member is provided with a second translation rod and an adjustment knob for adjusting the second translation guide member.

9. The apparatus of claims 7, further comprising a docking screw screwed through the second translation guide member for tightening the

second translation guide member against objects inserted into the cylindrical space formed by the annular second translation guide member.

10. The apparatus of claims 8, further comprising a docking screw screwed through the second translation guide member for tightening the second translation guide member against objects inserted into the cylindrical space formed by the annular second translation guide member.

11. A method of fixating an eye cornea for surgery, comprising:

placing an eye fixation apparatus upon the eye globe conjunctiva around the cornea, wherein the eye fixation apparatus comprises an eye fixation portion with an annular convex bottom contact portion, said convex bottom contact portion including a concave bottom surface provided with criss-crossing channels, and a vacuum port connected to said eye fixation portion and in communication with said criss-crossing channels such that vacuum pressure applied to said vacuum port exerts vacuum pressure through such criss-crossing channels to pull the eyeball membrane to the criss-crossing channels; and

applying vacuum pressure to said vacuum port creating a pressure differential through said criss-crossing channels in relation to said conjunctiva, adhering said conjunctiva to said contact portion

bottom surface.

12. The method of claim 11, further comprising:

checking to see said eye fixation apparatus is centered around the cornea; and

shutting off the vacuum pressure if said eye fixation apparatus is not centered around the cornea, recentering said eye fixation apparatus, and reapplying said vacuum pressure.

13. The method of claims 11 or 12, wherein the eye fixation apparatus is further provided with adjustment arms connected to said eye fixation portion.

14. The method of claims 11 or 12, further comprising adjustably connecting a first annular translation guide member to the eye fixation portion to translate said first guide member laterally in relation to the eye fixation portion.

15. The method of claim 14, wherein the first translation guide member is adjusted using a first translation rod and a first adjustment knob.

16. The method of claim 13, further comprising tightening the first translation guide member against objects inserted into the cylindrical space formed by the first annular translation guide member with a docking screw threaded through the first translation guide member.

17. The method of claim 14, further comprising tightening the first translation guide member against objects inserted into the cylindrical space formed by the first annular translation guide member with a docking screw threaded through the first translation guide member.

18. The method of claim 14, further comprising adjustably connecting a second translation guide member to the first translation guide member to translate said second guide member in a direction non-parallel to the first guide member.

19. The method of claim 18, wherein the second translation guide member is adjusted using a second translation rod and a second adjustment knob.

20. The method of claim 18, further comprising tightening the second translation guide member against objects inserted into the cylindrical space formed by the second annular translation guide member with a docking screw threaded through the second translation guide member.

21. The method of claim 19, further comprising tightening the second translation guide member against objects inserted into the cylindrical space formed by the second annular translation guide member with a docking screw threaded through the second translation guide member.

22. An eye fixation apparatus, comprising:

an eye fixation portion, wherein the eye fixation portion has a low-profile annular convex bottom contact portion, said convex bottom contact portion including a concave bottom surface which goes upon the surface of an eyeball and encircles the cornea, and wherein the contact portion bottom surface is provided with criss-crossing channels;

a vacuum port connected to said eye fixation portion and in fluid communication with said criss-crossing channels;

a first annular translation guide member with a first translation rod and first adjustment knob, adjustably connected to the eye fixation portion, wherein the first translation guide member portion can translate laterally in relation to the eye fixation portion using said first adjustment knob acting upon said first translation rod;

a second annular translation guide member with a second translation rod and second adjustment knob, adjustably connected to the first translation guide member, wherein the second translation guide member portion can translate laterally in relation to the first translation guide member and eye fixation portion using said second adjustment knob acting upon second first translation rod;

a first and a second docking screw screwed through said first

and second translation guide members, respectively, and for tightening the first and second translation guide members against objects inserted into the cylindrical space formed by the first and second annular translation guide members; and

wherein, the profile of said eye fixation portion is substantially narrow so as to fit under the eye lid of a patient without use of a lid speculum.

EVIDENCE APPENDIX

The following evidence has been entered into the record and is relied upon in this Appeal:

Evidence 1. Affidavit under Rule 132, Dr. Brian R. Will, January 10, 2007.

(Entered in the record with the Request for Continued Examination filed January 12, 2007.)

Evidence 2. Affidavit under Rule 132, Dr. Brian R. Will, April 14, 2008.

(Entered in the record with the Request for Continued Examination filed April 14, 2008.)

Evidence 3. Publication, Jose L. Hernandez-Verdejo, Miguiel A. Teus, Jose M. Roman, Gema Bolivar, PORCINE MODEL TO COMPARE REAL-TIME INTRAOCULAR PRESSURE DURING LASIK WITH A MECHANICAL MICROKERATOME AND FEMTOSECOND LASER, *Investigative Ophthalmology & Visual Science*, January 2007, Vo. 48, No.1.

(Entered in the record with the Request for Continued Examination filed April 14, 2008 as Exhibit 1 to the Affidavit of Dr. Brian R. Will dated April 14, 2008.)

Evidence 4. Publication, Wei-Li Chen, Yung-Feng Shih, Shu-Lang Liao, Fung-Rong Hu, Por-Tying Hung, ULTRASOUND BIOMICROSCOPIC FINDINGS IN RABBIT EYES UNDERGOING SCLERAL SUCTION DURING

LAMELLAR REFRACTIVE SURGERY, *Investigative Ophthalmology & Visual Science*, December 2002, Vol. 43, No. 12.

(Entered in the record with the Request for Continued Examination filed April 14, 2008 as Exhibit 2 to the Affidavit of Dr. Brian R. Will dated April 14, 2008.)

Evidence 5. Publication, Alireza Mirshahi, MD, Thomas Kohnen, MD, EFFECT OF MICROKERATOME SUCTION DURING LASIK ON OCULAR STRUCTURES, *Ophthalmology*, April 2005, Vol. 112, Nr. 4.

(Entered in the record with the Request for Continued Examination filed April 14, 2008 as Exhibit 3 to the Affidavit of Dr. Brian R. Will dated April 14, 2008.)

Evidence 6. Publication, Christina J. Flaxel, MD, Young H. Choi, MD, Michael Sheety, MD, Stephen Christopher Oeinck, CRA, Joe Y. Lee, MD, Peter J. McDonnell, MD, PROPOSED MECHANISM FOR RETINAL TEARS AFTER LASIK, *Ophthalmology*, 2004; Vol. 111, pp. 24-27.

(Entered in the record with the Request for Continued Examination filed April 14, 2008 as Exhibit 4 to the Affidavit of Dr. Brian R. Will dated April 14, 2008.)

Evidence 7. Publication, Julie M. Albietz, PhD, Lee M. Lenton, Suzanne G. McLennan, DRY EYE AFTER LASIK: COMPARISON OF OUTCOMES FOR

ASIAN AND CAUCASIAN EYES, *Clinical and Experimental Optometry*, March 2005, vol 88.2.

(Entered in the record with the Request for Continued Examination filed April 14, 2008 as Exhibit 5 to the Affidavit of Dr. Brian R. Will dated April 14, 2008.)

Evidence 8. Publication, Jane-Ming Lin, MD, Yi-Yu Tsai, MD, RETINAL PHLEBITIS AFTER LASIK, *Journal of Refractive Surgery*, September/October 2005, Vol. 21, p.501.

(Entered in the record with the Request for Continued Examination filed April 14, 2008 as Exhibit 6 to the Affidavit of Dr. Brian R. Will dated April 14, 2008.)

Evidence 9. Publication, Jose M. Benitez-del-Castillo, M.D., Teresa del Rio, M.D., Teresa Iradier, M.D., Jose L. Hernandez, M.D., Alfredo Castillo, M.D., Julian Garcia-Sanchez, M.D., DECREASE IN TEAR SECRETION AND CORNEAL SENSITIVITY AFTER LASER IN SITU KERATOMILEUSIS, *Cornea*, January 2001, Vol. 20, pp. 30-32.

(Entered in the record by Examiner in Office Action dated April 17, 2007.)

EVIDENCE - 1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: BRIAN R. WILL

Serial No.	10/608,408	Examiner:	Shay, David M.
Filed:	June 27, 2003	Group Art Unit:	3735

For: EYE FIXATION APPARATUS

Date: January 10, 2007

Mail Stop RCE
The Honorable Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AFFIDAVIT UNDER RULE 1.132 TRAVERSING REJECTIONS

I, BRIAN R. WILL, hereby declare under penalty of perjury based on personal first hand knowledge the following to be true and accurate:

1. I write this declaration to overcome and traverse rejections made under Section 103 in the July 14, 2006 Final Office Action. This declaration is submitted in conjunction with a Request for Continued Examination.

2. I am a board certified Ophthalmologist with over 17 years of practice. I have performed over 28,000 LASIK procedures as well as over 10,000 other ocular procedures in that time, and currently perform over 3,000 LASIK procedures per year. I have intimate experience with much of what has been considered state of the art in the field of LASIK and other keratome procedures, using lasers and microkeratome blades, including the devices incorporating the Hellenkamp (U.S. 6,042,594), Clark (U.S. 5,591,174), Curtin

(U.S. 4,173,980) and L'Esperance (E.P. 0372127A1) references, or similar to these references, cited by the Examiner. This declaration is made based on my personal experience and that of my staff of two (2) ophthalmologists within the field.

3. My invention provides an improved apparatus and method for fixing the eye during keratome surgeries, and for adjusting surgical devices to the fixated eyeball during procedures. The improvements relate both to the improved accuracy of the surgery due to reduced distortion of the eyeball and greater precision of positioning, as well as reduced damage to the cornea, sclera and conjunctiva. These improvements are concrete. The improvement in outcomes includes: greater measured improvements in visual acuity for patients; less discomfort for patients during and after surgery; less damage to the cornea, sclera and conjunctiva during surgery; less discomfort for patients with narrow lid openings; and allows patients that have small lid fissures / apertures to undergo LASIK whereas existing technology denies them such an opportunity.

4. Regarding independent claims 1 and 11, a fundamental reason for the improved performance of the apparatus is the criss-cross channel design of the vacuum ring. The criss-cross channel design provides several specific benefits over existing devices:

a. The lands between the channels provide multiple contact points spread over a wider surface, preventing the cornea, sclera and conjunctiva from being displaced into the vacuum channels and providing a more stable contact, preventing "rocking" on the eye.

b. The use of criss-cross channels prevent occlusion of the vacuum source which can lead to loss of vacuum – and loss of eye fixation – during surgical procedures.

c. The use of criss-cross channels markedly reduces deformation of the eye and reduces intraocular pressure – thus it is safer, more comfortable, and provides improved accuracy, especially in Femtosecond procedures.

d. The use of criss-cross channels to distribute vacuum, rather than a vacuum annulus, creates a lower profile device thereby obviating the need to use a lid speculum, and providing more clearance in a tight space during procedures.

e. The surgeon is able to reposition the fixation device if the initial positioning is incorrect, because the criss-cross channels do not cause gross distortion of the cornea, sclera and conjunctiva, whereas existing devices prevent repositioning due to the indentation and elevation of a ring of tissue on the cornea, sclera and conjunctiva when conventional fixation devices are removed.

f. The use of shallow criss-cross channels allows for more rapid and thorough cleaning of the apparatus, providing quicker turnaround time between patients and extending the life of the devices themselves.

g. The addition of X-Y translation guides, see dependent claims 3-10 and 14-21, provide adjustment capabilities built in to the fixation device which allow for superior centration properties in laser procedures.

h. The addition of docking screws, see dependent claims 5, 6, 9, 10, 16, 17, 19, 20 and 21, for docking surgical devices into the fixation aperture, rather than conventional pincer type docking systems, provide smoother docking with less manual dexterity required.

5. The criss-cross channel design, claims 1 and 11, allows a lower vacuum setting to achieve the same fixation of the eye, and the narrowness and cross-orientation prevent significant displacement of the cornea, sclera and conjunctival tissue into the vacuum channels. Existing annular vacuum rings, such as taught by the Hellenkamp and Curtin references cited by Examiner, displace significant amounts of tissue into the vacuum ring cavity, leading to several drawbacks.

a. First, by drawing the ocular tissue into the annulus it can (and often does) damage the ocular tissue. Often this damage does not create problems, but under certain circumstances it can. In one example, if the initial setting of the fixation device is incorrect then the displacement can prevent repositioning because it leaves an indentation and a swollen ridge conforming to the annulus. The annular ring creates a ridge (rather like a "hickey") on the cornea, sclera and conjunctiva – the displaced ring of ocular tissue remains that way for some time. A second attempt at surgery can only be made after this annulus-shaped "hickey" has healed

because it prevents proper re-alignment of the vacuum ring itself. A second example of the problem created is when the displacement causes separation of the conjunctiva from the underlying scleral tissue – a condition called "chemosis." Some patients are more susceptible than others, but with the growth of LASIK and other surgical procedures this is becoming a more and more significant problem. Since the majority of inflammatory tissue in the eye is located in the conjunctiva, trauma to that tissue in the form of chemosis or, trauma in general, can significantly increase the amount of inflammation in the eye following surgery, which can lead to serious inflammatory complications such as Diffuse Lamellar Keratitis, that can markedly alter healing and the surgical result. A third example of problems resulting from conjunctival displacement is that, even without a complete separation such as in chemosis, the damage caused by conjunctival displacement can lead to subconjunctival hemorrhaging, which appears as a red blood spot on the eye. Although not generally dangerous, it is undesirable for the patient (and a poor advertisement for surgeons).

b. The apparatus and method described in claims 1 and 11 reduce these risks in several ways. First, the criss-cross channels are shallow and distributed over a wide area which conforms to the shape of the eyeball, because they are surface grooves rather than an annulus. Second, the separate channels pull the corneal, conjunctival and scleral surface taught between them and provide many lands, conforming to the

natural shape of the eyeball, for contact area. In other words, rather than being drawn into the channels the corneal tissue is held against the lands, resulting in minimal displacement. Third, because the channels are spread over a wide area rather than a narrow ring a lower vacuum pressure can be used to achieve the same stability. The ability to hold the eyeball in place is determined by both the vacuum pressure multiplied by the total area of the channels or annulus (i.e. the absolute force applied), as well as the depth over which the force is distributed (i.e. the wider the base of application, the more stable the support provided by the fixation apparatus – proportional to the moment of inertia). Therefore, multiple points of contact spread over a wider band create a more stable base than narrower annular vacuum rings, or conversely, lesser vacuum pressure is required to achieve comparable stability – which in turn reduces the likelihood of all the complications associated with vacuum fixation devices. For example, the apparatus and method of claims 1 and 11 requires lower vacuum levels than for conventional annular devices, using the system described in Hellenkamp, that I have significant experience with. Although the L'Esperance reference, cited by Examiner, is an improvement over annular designs in this last regard, the porous membrane of L'Esperance is subject to clogging (see ¶ 9, below), and the annular vault necessitates a lid speculum (see ¶¶ 7-8, below).

c. A second advantage of the apparatus and methods of claims 1 and 11 is that they avoid the excessive deformation of the

eyeball, and consequently the cornea, during a LASIK or other keratome procedure, which is caused by annular vacuum rings. This deformation leads to dual problems of less accurate correction due to the distorted cornea, and raised pressure within the eye which can lead to more dangerous complications such as occlusion of the blood supply. The high vacuum and eyeball distortion caused by annular rings frequently result in the cornea being compressed so that it is thinner than normal and it also assumes a completely abnormal shape and contour. Although the eye is somewhat elastic, it does not immediately rebound to its natural shape or thickness after the vacuum or vacuum ring is released. The eyeball distortion and occlusion of the arterial blood supply also renders the iris to be temporarily ischemic, thereby temporarily altering its shape and the normal pupil response time to light and accommodation. These distortions of normal eye conditions are important factors in less than optimal surgical outcomes.

d. In addition, this distortion and compression alters the normal water content of the cornea from its natural state. The accuracy of the LASIK procedure depends on three primary factors: accurate cutting of the keratome flap, accurate placement and control of the Femtosecond and excimer lasers, and the shape and condition of the cornea when it is lazed. Excimer lasers used to photoablate corneal tissue assume a normal state of corneal hydration as well as a predictable corneal contour and shape. Individual variations in the water content of the cornea caused

by corneal compression from the annular vacuum ring cannot be predicted or accounted for by the excimer lazing processes. In addition, most excimer lasers require that the ablation profile be modified on an individual basis to account for the angle of incidence of the excimer beam at the exact point of beam application on the curved corneal surface. Because the annular vacuum ring deforms the eye and the tissue is not immediately elastic following ring removal, the exact shape of the contour to the cornea is no longer known and attempts to precisely compensate for angle of incidence effects on excimer beam efficiency based upon preoperative corneal shape measurements are no longer accurate or valid.

e. Compression of the corneal tissue, caused by annular vacuum rings, also creates errors in creating a predictable flap thickness, as current Femtosecond and keratome devices determine flap depth by measuring from the anterior surface of the cornea only. Tissue compression of the anterior corneal tissue or the entire cornea of only a few microns will cause such a device to create a flap that is significantly thicker than expected. Excessively thick or unpredictable flap thickness is one of the leading sources of error in LASIK surgery and predisposes the subject eye to structural weakness and risk for ectasia. Eye tracking excimer lasers frequently use the iris and pupil as a landmark for reference for the tracking apparatus so as to compensate for intraocular eye movement and as a point reference for the centration of wavefront or topographically guided photoablation procedures. Subjecting the iris to

transient ischemia by high intraocular pressure from annular vacuum rings intraoperatively distorts the pupil and renders the iris less responsive to light and accommodation for a temporary period. These factors measurably reduce the accuracy of centration and thereby adversely effect the accuracy of the refractive treatment.

f. Therefore, based on these various factors: (1) preoperative measurements of corneal thickness, hydration state and contour are not accurate after the eyeball has been grossly deformed by high vacuum pressures; (2) flap thickness based on depth measurements from the anterior surface of the cornea after the tissue is compressed and distorted can no longer accurately predict flap thickness postoperatively; (3) distortion and distention of the iris and pupil due to transient iris ischemia introduces significant error in centration of the intended photoablative procedure as the pupil centroid is displaced from the normal preoperative position; and, (4) the excimer laser can no longer accurately compensate for tissue shape or tissue hydration consistency during the procedure as these factors have been modified intraoperatively by high vacuum. All of these factors create the propensity towards unpredictability of refractive endpoint and cause over and under corrections of the refractive error. Fixation devices such as Hellenkamp and Curtin cause unnecessary deformation: after sucking the sclera up into the vacuum chamber the targeting device flattens the cornea down, compressing the tissue and thereby introducing deformation error.

g. Hellenkamp specifically teaches that the annular-style vacuum ring "cause[s] the cornea to be urged upwardly and to protrude through the aperture 25 of the positioning segment 20..." *See Hellenkamp, col. 7, ll. 30-32.* Claims 1 and 11 significantly reduce the distortion due to the distributed vacuum channels. Lower vacuum is required to begin with since the channels are interspersed between surfaces which approximate the eye's natural shape, so the tissue is held against these lands. Minimal displacement of the cornea into the vacuum channels reduces the distortion of and pressure within the eyeball. And, the use of channels rather than a porous surface prevents clogging which can cause some areas to be held more tightly than other areas – leading to still more distortion as well as other potential complications (discussed below).

h. A third advantage of the apparatus and method of claims 1 and 11 is that the criss-cross channels are less susceptible to occlusion from displacement of the conjunctiva, sclera or cornea into the annulus and from mucus. Partial occlusion can result in some areas being held more tightly than others making those more tightly held areas more susceptible to chemosis or other trauma. Occlusion may also result in loss of vacuum during the surgical procedure with potentially devastating consequences. The Hellenkamp reference, cited by Examiner, specifically discusses some problems caused by displacing the sclera into annular rings, and attempts to solve these problems. The vacuum enhancer of

Hellenkamp is a partial solution to the problem of occlusion, making loss of vacuum less likely, but does not address the other drawbacks of annular designs discussed above. The sclera is still exposed to a continuous hollow annular chamber thereby causing a raised ring on the tissue. The hollow annulus also imposes a high profile, similar to L'Esperance, requiring a lid speculum and attendant disadvantages discussed above at paragraphs 7-8, below. Hellenkamp's solution is limited by the fact that it relies on modifying a conventional annular vacuum ring structure. Hellenkamp, at col. 3, ll. 20-44, discusses displacement of the conjunctiva into an annular chamber and problems of conjunctival separation and damage. Hellenkamp, at col. 3, ll. 20-44, discusses problems of vacuum chamber occlusion caused by displacement of the conjunctiva into the vacuum ring chamber. Hellenkamp, at col. 3, ll.45-61, discusses problems of mucus buildup in annulus-type rings and difficulty in cleaning due to the hardening of residual mucus debris. If buildup and hardening of mucus within an open channel is problematic, as taught by Hellenkamp in 1998, due to the inability to clean out the annulus chamber, then buildup and hardening of mucus is even worse in a porous surface such as taught by L'Esperance in 1988. Residual mucous material embedded in this porous material may introduce unwanted complications from cross contamination between patients, even despite sterilization procedures. Proteins, other biological macromolecules and debris transferred between patients from this porous

membrane that contacts sensitive eye tissue will increase postoperative inflammation and potential infection from viral, bacterial or prion residues. There is simply no effective way to clean the pores taught by L'Esperance so, in a relatively short time, the device will become unusable and require replacement. The apparatus and method of claims 1 and 11 reduce the likelihood of occlusion – through the use of cross-connected vacuum channels – and significantly reduce the other negative effects inherent to annular designs, as discussed above. The criss-cross channels are less subject to blockage because if one channel becomes blocked – for whatever reason – an alternate vacuum path remains. The criss-cross channels are significantly easier to maintain and clean because they are flat and shallow, rather than the vaulted annulus of existing devices.

i. Applicant does not argue that Hellenkamp, L'Esperance or any other reference cited, is non-functioning or invalid. Rather, Applicant through claims 1 and 11 provides unobvious solutions to verified real world problems.

6. The Examiner's Office Action of July 14, 2006, at page 2, states that since the L'Esperance patent states that it only claims to operate "solely upon the optically used area of the anterior surface of the cornea" (Examiner quoting the L'Esperance reference) then damage to the cornea due to the fixation device would "constitute operating on a portion of the eye which was other than the optically used portion of the cornea." I am an ophthalmologist and the Examiner's statement is incorrect – complications from surgery are not

"operating", they are complications. The recognition that a surgical procedure has side effects caused by the surgical devices does not render the side effects – unwanted and unintended – "operating." The Examiner's statement is even more perplexing considering the fact that the Hellenkamp reference, cited by Examiner, discusses some of the problems of corneal damage caused by annular vacuum rings at length. Hellenkamp attempted one method of solution, which turns out to be inadequate in certain critical respects. The goal of my invention, described in claims 1 and 11, which is actually achieved, is to reduce unwanted side effects and complications from surgery, and provide greater accuracy during surgery.

7. The criss-cross channels of my claims 1 and 11 reduce the potential for trauma to the cornea, a leading cause of post-LASIK complications. The incidence of subconjunctival hemorrhage has been estimated as high as 10% or more in LASIK patients. Thus, the problems associated with existing eye fixation apparatus are far from "speculative," as asserted by the Examiner, who provided no references to back up his incorrect assertions of fact. *See, e.g.,* Sun L, Liu G, Ren Y, Li J, Hao J, Liu X, Zhang Y., EFFICACY AND SAFETY OF LASIK IN 10,052 EYES OF 5081 MYOPIC CHINESE PATIENTS. *Journal of Refractive Surgery,* 2005 Sep-Oct; 21(5 Suppl):S633-5. PMID 16212294.

8. The low profile achieved by the criss-cross channel design eliminates the need for a lid speculum in most cases, including patients with narrow ocular fissures and orbits. Higher rates of complications from using annular fixation devices on patients with narrow ocular fissures and orbits, such

as patients of Asian descent, have been documented in medical studies. In at least one peer-reviewed study approximately 28% of Asian LASIK patients experienced prolonged or permanent "dry eye" following LASIK procedures. *See, e.g.,* Albietz JM, Lenton LM, McLennan SG., DRY EYE AFTER LASIK: COMPARISON OF OUTCOMES FOR ASIAN AND CAUCASIAN EYES, *Clinical and Experimental Optometry* 2005 Mar; 88(2):89-96. The study concluded that this was likely due, in part, to damage from the vacuum fixation apparatus caused by the tight fit of the suction ring and keratome device within their narrower orbits. Id, p.95. The criss-cross channels obviate much of this risk. The criss-cross channel design imposes fewer stresses on the cornea and eyeball to begin with. This design also allows use of a low profile, conforming, base which fits under the eyelid, rather than an annular vault, obviating the need for a lid speculum, which is required when using apparatus taught by Hellencamp, L'Esperance, and Curtin. Even in the absence of dry eye complications, lid specula carry the disadvantages of causing greater discomfort to the patient both during and after surgery, and creating space interference for the surgical team in an already tight working space.

9. I have reviewed the L'Esperance references cited by the Examiner, including the newly cited references (US 4,732,148 and US 4,770,172). All the L'Esperance references specifically claim annular vacuum designs applying suction through a permeable (i.e. porous) membrane, and thus all share the drawbacks of the high profile and difficult cleaning requirements of other annulus apparatus. Based on my experience the pores of the L'Esperance design are

quite vulnerable to clogging – as is the case with any porous membrane applied to mucus surfaces. I have found, based on extensive experience in thousands of surgical procedures, that devices such as that taught by L'Esperance have at least two major drawbacks that are not mere "speculation."

a. First, L'Esperance relies on applying suction through a porous surface backed by an annular chamber. The porous surface is subject to clogging by mucus from the conjunctiva surface – all porous surfaces are subject to clogging. This clogging in turn leads to the dual problems of causing blockage of the vacuum path and inadequate cleaning which shortens useful life. Mucus is difficult or impossible to clean out of porous surfaces, especially so after hardening, so the porous membrane device taught by L'Esperance would either have a very short useful life or it would require special cleaning procedures which would make surgical procedures significantly less economical. It is also anticipated that cross contamination from residual mucous material, bacteria and other biological macromolecules in the porous material would introduce significant risk to patients from infection and excessive postoperative inflammation from the transference of foreign biological molecules and material between patients. The Hellenkamp reference discusses the difficult problem of cleaning mucus and attempts to solve the problem by making part of his device disposable – a less than optimum solution. In addition to the danger of loss of vacuum, or uneven vacuum, if the pores become completely clogged during a procedure (due

to inadequate cleaning or other factors) the membrane will adhere to the corneal surface through surface tension of the mucus and water, which could easily cause damage when removed. (As an example, place a wet glass on a smooth surface or coaster – when it is lifted the coaster will adhere to the bottom of the glass.) This kind of force applied to the corneal surface – a delicate structure – can and will cause damage. This danger is especially pronounced in patients who are susceptible to chemosis or have abnormally poor adhesion of the epithelial layer such as a Basement Membrane Dystrophy, which is a very commonly occurring anomaly.

b. A second drawback of the L'Esperance reference, shared by other references cited by the Examiner, is the high profile of the vacuum chamber vault necessitated by annular designs. The high profile requires use of a lid speculum during procedures in order to hold the eyelids back. In a patient with narrow lid fissures, a high-profile vacuum ring such as L'Esperance may not be able to be used at all, with or without a lid speculum. Lid specula increase risks of complications, create more discomfort for the patient and are additional interference in a constrained space requiring significant precision for a successful procedure. The discomfort caused by the high profile apparatus is especially pronounced for patients with narrow lids (see ¶¶ 7 & 8, above). The criss-cross channels solve this problem, which is a real problem, because they create a low profile that can fit under a patient's lid.

10. The X-Y translation capability built in to the eye fixation apparatus, (claims 3-10 and 14-21) and the use of docking screws rather than conventional pincers (claims 5,6, 9, 10, 16, 17, 20 and 21), are also major improvements over the state of the art. The X-Y adjustment capability allows the laser or other surgical apparatus to be slaved to the eyeball, rather than vice versa (e.g. as shown in the Curtis reference, cited by Examiner). Use of translation rods with adjustment knobs, directly on the eye fixation device, greatly reduces the manual dexterity required for adjustments, and provides for more accurate docking of the surgical apparatus. The improvement has been significant, especially in Femtosecond procedures, in achieving superior centration properties.

a. The X-Y translation capability and use of docking screws provides other advantages as well. No fixation device will achieve perfect alignment on a patient's eye. Existing eye fixation devices, represented by Hellenkamp, Curtis and L'Esperance, don't adjust to the eyeball, so surgeons either have to force the eye into alignment by manipulation of the fixation apparatus or, in the case of Femtosecond laser surgery, the laser controls must provide for complicated adjustment capabilities to compensate for x-y offset. Forcing the eye into alignment by manually distorting the fixation apparatus magnifies all of the problems with eye distortion discussed above. Attempting to correct for gross distortions through laser controls requires complicated hardware and software which is expensive and potentially prone to problems. In addition, for microkeratome procedures no adjustment is possible without the x-y

translation capability. The only adjustment provided is for depth of the blade.

b. The x-y translation capability of claims 3-10 and 14-21 allows the surgeon to dock the laser or other apparatus into the fixation device, and make simple adjustments using the docking screws (claims 5,6, 9, 10, 16, 17, 20 and 21) while sighting to an eye with minimal distortions.

c. The addition of adjustment arms, as in claims 2, 13 and 22 allow a surgeon to easily maneuver the device on the eye surface without their fingers obscuring their vision. Additionally, because the surgeon's fingers are holding the adjustment arms – i.e. away from the actual conjunctival surface – there is less chance of scratches or contamination due to inadvertent contact.

11. The experience of myself and my staff has demonstrated the need for these improvements. One must appreciate that ophthalmologic surgery using lasers to reshape the eye, or perform other procedures, frequently involves adjustments in the sub-micron range, so seemingly minor improvements to surgical apparatus can produce significant improvements in patient outcomes and economies. I would not have expended the time, effort and money to develop this new invention if existing devices were fully adequate and did not exhibit known adverse affects upon tissue health and healing during refractive eye surgery procedures..

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

DATED THIS _____ January 12, 2007
BRIAN R. WILL, MD

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EVIDENCE - 2

US PATENT APPLICATION
Docket No. WILB01

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: BRIAN R. WILL

Serial No.	10/608,408	Examiner:	Shay, David M.
Filed:	June 27, 2003	Group Art Unit:	3735

For: EYE FIXATION APPARATUS

Date: April 14, 2008

Mail Stop RCE
The Honorable Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AFFIDAVIT UNDER RULE 1.132 TRAVERSING REJECTIONS

I, BRIAN R. WILL, hereby declare under penalty of perjury based on personal first hand knowledge the following to be true and accurate:

1. I write this declaration to overcome and traverse rejections made under Section 103 in the April 11, 2007 Final Office Action. This declaration is submitted in conjunction with a Request for Continued Examination. Applicant timely filed a Notice of Appeal on June 22, 2007, and timely filed Appeal Briefs, but has withdrawn the Appeal in order to submit new evidence into the record for consideration.

2. I have previously submitted a declaration under Rule 1.132, dated January 10, 2007. I reiterate the statements and arguments made in that prior declaration and hereby incorporate those statements by reference.

3. I am a board certified Ophthalmologist with over 17 years of practice. I have performed over 28,000 LASIK procedures as well as over 10,000 other ocular procedures in that time, and currently perform over 3,000 LASIK procedures per year. I have intimate experience with much of what has been considered state of the art in the field of LASIK and other keratome procedures, using lasers and microkeratome blades, including the devices incorporating the features of Hellenkamp (U.S. 6,042,594), Clark (U.S. 5,591,174), Curtin (U.S. 4,173,980) and L'Esperance (E.P. 0372127A1) references, or similar to these references, cited by the Examiner. This declaration is made based on my personal experience and that of my staff of two (2) ophthalmologists within the field, whom I personally supervise.

4. My staff ophthalmologists and I meet regularly to discuss patient outcomes and to evaluate procedures and conduct training.

5. The Examiner has expressed skepticism that prior art devices using annular vacuum rings such as described in Hellenkamp cause complications in patients undergoing LASIK and other surgical procedures. My descriptions of the drawbacks of existing known devices are not "speculative", but are a subject of growing concern with an increasing body of research and literature investigating these issues.

6. Attached as Exhibit 1 is a true and correct copy of an article, Jose L. Hernandez-Verdejo, Miguiel A. Teus, Jose M. Roman, Gema Bolivar, PORCINE MODEL TO COMPARE REAL-TIME INTRAOCULAR PRESSURE DURING LASIK WITH A MECHANICAL MICROKERATOME AND FEMTOSECOND LASER, *Investigative*

Ophthalmology & Visual Science, January 2007, Vo. 48, No.1. The intent of the authors was to compare the elevation of intraocular pressure (IOP) caused by the flap-cutting portion of LASIK procedures using a mechanical microkeratome blade versus laser microkeratome cutter. At page 1, the authors note that there is a widespread concern about the damage caused to eye structures from the increased IOP during LASIK and other procedures. The authors note that several hypothesis focus on the "suction ring" used to fix the eye during procedures. "Different hypotheses explain the posterior segment complications, with the first postulating that the mechanical stress is caused by the IOP elevation produced by the pneumatic suction ring, which may induce tangential stress on the posterior segment." Id at p.68, col 2. The authors note that real-time measurement of changes in IOP during LASIK and other procedures have been difficult to measure in the past. Id. During the experimental procedures the IOP of the porcine eyeballs was recorded continuously. Id at p. 69, col 2. "Both groups [mechanical and laser flap cuts] had an IOP increase immediately after the placement of the suction ring that was maintained during the entire surgical procedure." Id p.70, col 2. The authors noted another study which demonstrated analogous significant rises is IOP using single-port versus two-port suction rings. Id at p.70, col 2. The authors' noted that "...pressure setting for the suction ring is an important variable in determining consistent corneal flap thickness during LASIK" and that lower vacuum settings tend to produce lesser increases in IOP. Id. pp. 70-71. "Sudden increases in IOP, although well tolerated, may induce changes in the peripheral retina... These possible posterior segment

complications, among others, make the knowledge of the exact IOP increase induced by surgical procedures such as laser refractive surgery increasingly important."

a. The authors do not specify that the suction rings used were based on Hellenkamp, but in the field of ophthalmologic surgical procedures the term "suction ring" is generally understood to refer to a vacuum annulus design, essentially the same as taught in Hellenkamp. Vacuum annulus designs are the industry standard at this time.

7. Attached as Exhibit 2 is a true and correct copy of an article, Wei-Li Chen, Yung-Feng Shih, Shu-Lang Liao, Fung-Rong Hu, Por-Tying Hung, ULTRASOUND BIOMICROSCOPIC FINDINGS IN RABBIT EYES UNDERGOING SCLERAL SUCTION DURING LAMELLAR REFRACTIVE SURGERY, *Investigative Ophthalmology & Visual Science*, December 2002, Vol. 43, No. 12. The purpose of the study was to evaluate changes in corneal structure caused by changes in IOP due to application of scleral suction rings. Suction ring related complications during lamellar refractive surgeries (including LASIK) included retinal vascular occlusion, ischemic optic neuropathy, and macular hemorrhages due to elevated IOP during surgery, and subconjunctival hemorrhage – caused by application of the suction ring. Id at 3669, col 1. The authors concluded that the application of the suction ring itself causes harm to a subject's eye, and that the amount of damage correlated to the length of time the suction ring was applied. The damage was due to the stresses induced by the deformation of the eye itself and

consequent rise in IOP, as well as the effect of the suction ring on the scleral surface displacing into the suction ring volume. Id at pp. 3670-71.

8. Attached as Exhibit 3 is a true and correct copy of an article, Alireza Mirshahi, MD, Thomas Kohnen, MD, EFFECT OF MICROKERATOME SUCTION DURING LASIK ON OCULAR STRUCTURES, *Ophthalmology*, April 2005, Vol. 112, Nr. 4. The purpose was, "To study the effect of microkeratome suction on ocular structures during LASIK." The procedures were conducted using a 20.3 mm suction ring. Id at p.646, col 1. "The mechanics of microkeratome suction can be compared to that of blunt ocular trauma when the ocular globe is compressed and quickly released... however, at a much lower level incidence and degree." Id at p.648, col 2. The authors noted that more study is required to understand the precise causes. Thus, this article corroborates my belief that existing suction ring designs are a source of trauma to the eyes of patients undergoing LASIK procedures. My invention addresses what I believe to be part of the cause of this trauma – the displacement of the sclera into the high chamber of suction ring designs such as Hellenkamp, and the deformation of the eyeball caused by these designs, which draw the eyeball up and into the central opening for cutting of the keratome flap.

a. The authors describe increased IOP as desirable "creating a firm cornea and permitting a precise corneal flap to be cut, which is followed by laser ablation." Id at p.645. Thus, the conventional literature can be said to teach away from my invention, in that my design seeks to reduce eyeball

deformation and minimize the rise in IOP caused by the eye fixation device.

9. Attached as Exhibit 4 is a true and correct copy of an article, Christina J. Flaxel, MD, Young H. Choi, MD, Michael Sheety, MD, Stephen Christopher Oeinck, CRA, Joe Y. Lee, MD, Peter J. McDonnell, MD, PROPOSED MECHANISM FOR RETINAL TEARS AFTER LASIK, *Ophthalmology*, 2004; Vol. 111, pp. 24-27. The suction ring used in the study was described: "The suction ring is a circular chamber that fixates the eye by means of a vacuum. The underside of the fixation ring has a vacuum chamber that seals against the globe." Id at p. 26, col. 1-2. This matches the description of the devices in Hellenkamp and Curtin/Clark and is indicative of existing devices. The authors concluded that the mechanics of the suction ring itself may be a source of damage to eyes of patients with pre-existing vulnerabilities.

10. Attached as Exhibit 5 is a true and correct copy of an article, Julie M. Albietz, PhD, Lee M. Lenton, Suzanne G. McLennan, DRY EYE AFTER LASIK: COMPARISON OF OUTCOMES FOR ASIAN AND CAUCASIAN EYES, *Clinical and Experimental Optometry*, March 2005, vol 88.2. The purpose was to investigate anecdotal evidence that LASIK patients of Asian decent experienced higher incidences of complications such as Dry Eye after LASIK. The authors found that Asian LASIK patients did suffer higher incidence of dry eye, with several potential contributing causes. One cause discussed was the smaller ocular orbit and tighter lids generally found in Asian patients compared to Caucasian patients. Id at p. 95. The tighter lid structure led to a higher incidence of flap cut

complications and longer intra-operative prep times leading to greater damage to the ocular surface were due in large part to the tight fit of the suction ring between the lids. Id at p. 95.

a. Applicant submits that one of the advantages of the low profile apparatus of the present Application is that it fits under the eyelids of patients. Thus, the lids must accommodate only the narrow central access hole for the microkeratome blade or laser access (approximately 9-12mm) rather than the full diameter of the vacuum ring (approximately 20mm +/-, see Exhibit 3 and paragraph 7, above).

b. Longer intraoperative prep times translates into longer application of vacuum to the suction ring, which as discussed in Exh. 2 and paragraph 6, above, seems to lead to increased trauma to the ocular surface and anterior structures.

11. Attached as Exhibit 6 is a true and correct copy of an article, Jane-Ming Lin, MD, Yi-Yu Tsai, MD, RETINAL PHLEBITIS AFTER LASIK, *Journal of Refractive Surgery*, September/October 2005, Vol. 21, p.501. The authors provide a case study of a patient suffering retinal phlebitis due to LASIK complications. The authors concluded that the cause of the retinal phlebitis may have been due to the negative effects of elevated IOP caused in part by the

suction ring. The authors note that standard practice is to achieve an IOP of at least 65mmHg to support mechanical keratome flap cutting. Id at 502, col 2.

12. The Exhibits discussed above, as a whole, demonstrate that the existing industry suction rings, which are essentially versions of those described in Hellenkamp and Curtin/Clark, are known to be problematic in LASIK procedures although this was not known at the time of the Hellenkamp reference. The present invention seeks to reduce the damage caused by suction ring devices such as described in Hellenkamp, which are commonly used in ophthalmologic surgery.

13. Regarding the porous membrane and high profile chamber of L'Esperance, I am of the opinion, based on over 17 years of experience in the field and having personally performed thousands of LASIK procedures, and having trained and supervised dozens of other doctors in the procedures, that the porous membrane system is subject to a number of drawbacks. Among other things, it is my professional opinion that the porous membrane with vacuum on one side and mucus on the other would be subject to frequent clogging and be difficult or impossible to properly clean and sterilize. The fact that, with extensive personal experience in this field, I am not familiar with any vacuum fixation device using the L'Esperance porous membrane system supports my opinion. If the L'Esperance membrane were effective then surgeons would use it, and I have not seen surgeons use such a device. The nature of the L'Esperance device also requires a high profile vacuum chamber. That is what is taught by L'Esperance and I see no other way to use the L'Esperance system without

extensive modifications. Therefore, all of the problems I have described, and which are supported in the professional literature, relating to high profile devices would apply especially to L'Esperance.

14. I also address the Examiner's prior stated skepticism regarding the need for lid specula when using high profile suction rings such as described in Hellenkamp, Curtin/Clark and L'Esperance. A high profile suction ring will actually not fit into many patients' eyes as their lid fissures are simply not large enough to accept the diameter or high profile vacuum ring required. The vacuum fixation device described in L'Esperance appears to have even worse features. The inability to accept high profile suction rings is particularly true for patients of Asian descent, and smaller people (females more frequently than males). With high profile apparatus described in Hellenkamp and L'Esperance the surgery either cannot be performed on such patients, or the patient must have their eyelids cut open and then sutured back together at the completion of the surgery. This significantly increases the risk of the surgeries, and leads to longer healing times for the patients.

15. In many, many cases where the lids are very tight, although we can complete the surgery, the patient experiences excessive pain because we have had to stretch the lid tissues in order to place the suction ring. This stretching may lead to permanent damage to the delicate lid tissue (skin, tendons and muscles) and result in development of "droopy" lids or redundant skin on the eyelids over the longer term. Such conditions would require additional surgery to repair. These are medical facts that any experienced refractive surgeon would be

aware of and are outlined to the patient in every surgical consent form. In contrast, the low profile vacuum ring of the present Application allows much of the footprint of the vacuum fixation device to be inserted *under* the lids, thereby allowing surgery to be performed without these difficulties or long term risks. The low profile is achieved through the use of the criss-cross vacuum channels, which are elements of all claims. Claim 22 explicitly claims a low profile apparatus, with criss-cross channels, which fits under the eyelid to obviate the need for a lid speculum.

16. Other problems with high profile suction rings, such as described in Hellenkamp and L'Esperance, lead to difficulties in carrying out the surgery itself. A high profile suction ring allows the patients' eyelids to gain more purchase, or force, on the ring. In a patient that is squeezing hard, they may dislodge the ring during the operation, which can result in irreversible eye damage in the worst case. As a result, a lid speculum is nearly mandatory when using suction rings described in Hellenkamp and L'Esperance so as to control lid pressure. The low profile device described in the present Application causes a lower level of distention of the sidewall of the eye, so the patient will not likely feel the same level of pain or pressure and so will be less likely to squeeze their lids together (and therefore less likely to displace the suction ring and less likely to cause long term damage to the lid tissues). Equally important, the eye lids cannot obtain the same level of tension on the edge of the low profile vacuum ring and this markedly diminishes the need for a lid speculum and reduces the potential for

serious intraoperative complications. The low profile device avoids this because eye lid slips comfortably over the vacuum footprint of the device.

17. The low profile of my apparatus, as described in the claims, is achieved through the use of the criss-cross channel design. The criss-cross channels allow the use of shallower vacuum channels and distribute the vacuum over a greater area, allowing reduced vacuum levels. The Exhibits 1-6, discussed above, all discuss the damage caused to the eye structures by higher vacuum applied through suction rings similar to Hellenkamp.

18. I would also like to address an issue which I have not previously addressed. The present literature, such as discussed in Exhibits 1-6, addresses both the damage caused by elevated IOP, as well as the desirability of elevated IOP in order to tension the cornea for cutting the flap. My invention teaches an opposite approach – to improve the accuracy of flap cuts and corneal shaping by minimizing the increase in IOP during the vacuum fixation and flap cutting portion of the procedure. As I have explained previously, the present apparatus and methods seek to achieve higher accuracy by reducing distortion of the eyeball and changes in hydration of the cornea caused by suction rings such as described in Hellenkamp. Thus, the references cited by the Examiner actually teach away from the apparatus and methods which I am claiming.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that

willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

DATED THIS April 14, 2008

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EVIDENCE - 3

Porcine Model to Compare Real-Time Intraocular Pressure during LASIK with a Mechanical Microkeratome and Femtosecond Laser

José L. Hernández-Verdejo,[1,2] *Miguel A. Teus,*[1,3] *José M. Román,*[1] *and Gema Bolívar*[3]

Purpose. To compare real-time intraocular pressure (IOP) during laser in situ keratomileusis (LASIK) in porcine eyes using two types of microkeratomes.

Methods. An interventional, prospective study of two microkeratomes: a Moria 2 (Moria group) and an IntraLase femtosecond laser (IntraLase Corp., Irvine, CA; IntraLase group). These devices were used to create lamellar corneal flaps in freshly enucleated porcine eyes. The IOP changes induced by the procedures were recorded with a reusable blood pressure transducer connected to the anterior chamber by direct cannulation.

Results. Seven porcine eyes were studied in each group. The IOP increased during the suctioning phase, reaching a mean of 122.52 ± 30.40 and 160.52 ± 22.73 mm Hg during the cutting phase in the Moria group (the total time in this group was 36.42 ± 7.48 seconds; suctioning required 21.42 ± 7.48 seconds and the cutting phase, 15 ± 2.88 seconds). In the IntraLase group, the IOP reached 89.24 ± 24.26 mm Hg during the suctioning phase and 119.33 ± 15.88 mm Hg during the intrastromal laser application (the total time was 92.85 ± 13.49 seconds; suctioning required 40.00 ± 9.57 seconds and the cutting phase 52.85 ± 5.66 seconds). Both IOPs during both phases differed significantly between the two groups ($P = 0.01$ for all comparisons).

Conclusions. Real-time IOP can be measured during LASIK using a transducer connected to the anterior chamber. The results showed a significant increase in IOP during the procedure in both groups, although with the IntraLase the IOP seemed to increase to a lesser extent than with the conventional mechanical microkeratome. (*Invest Ophthalmol Vis Sci.* 2007;48:68–72) DOI:10.1167/iovs.06-0192

Laser in situ keratomileusis (LASIK) has become the most frequently performed corneal refractive surgery for the correction of low to moderate myopia. The procedure involves preparation of a superficial flap by using a mechanical keratome and ablation of the corneal stromal tissue with an excimer laser.[1]

Femtosecond laser technology enables nonmechanical creation of a corneal flap.[2–4] This technology includes a solid-state laser used to create flaps during LASIK. The laser uses an infrared wavelength (1053 nm) to deliver closely spaced 3-μm spots that can be focused to a preset depth to photodisrupt tissue within the corneal stroma. The resultant plasma produces cavitation bubbles, consisting primarily of water and carbon dioxide. The IntraLase femtosecond laser system (IntraLase, Corp., Irvine, CA) relies on a low-pressure (35 mm Hg) suction ring to align and stabilize the globe. A flat lens attached to the laser delivery system is used to applanate the cornea within the suction ring. To create the ideal corneal flap during LASIK, sufficiently high intraocular pressure (IOP) is needed to manage the eye.

Two different ways to measure IOP during corneal refractive surgery have been proposed; both have some drawbacks. Applanation tonometry cannot be performed when the microkeratome is cutting the flap. In addition, the viscosity of the vitreous gel may jeopardize IOP measurement in direct cannulation of the vitreous cavity.[5–7] For this reason, we recorded the real-time IOP by direct cannulation into the anterior chamber, to obtain accurate IOP measurements during LASIK.

The real intraoperative IOP that is achieved during the suctioning and the cutting phases and the differences in IOP that can occur if the flap is created with a mechanical keratome or with the IntraLase femtosecond laser have not been measured during surgery. High IOP and sudden changes in IOP may cause irreversible changes in ocular tissue.

The anterior segment complications of LASIK have been well documented in the literature.[8] In addition, there have been several reports proposing a casual relationship between LASIK and retinal detachments in myopic eyes[9–11]; macular hemorrhages, macular holes, lacquer cracks, and choroidal neovascular membranes developed after LASIK have also been reported.[12] Different hypotheses explain the posterior segment complications, with the first postulating that the mechanical stress is caused by the IOP elevation produced by the pneumatic suction ring, which may induce tangential stress on the posterior segment.[13] Some investigators have proposed that the shockwave generated by the impact of the excimer energy on the cornea can generate pressure of up to 100 atmospheres, which also causes mechanical stress on the eye.[14] Acute damage to the optic nerve after LASIK has also been reported.[15]

Some case studies have reported that this increase in IOP damages the retinal ganglion cells, causing visual field defects.[16] Other studies have reported that the retinal nerve fiber layer thickness decreases after uncomplicated LASIK[17,18] or even that LASIK could cause occlusion of the retinal arteries.[19]

To the best of our knowledge, there are no published studies of the real-time IOP changes during a femtosecond laser procedure compared with IOP changes induced during a conventional mechanical LASIK procedure, especially when the IOP is measured via the anterior chamber.

The purposes of this study were to develop an experimental model to measure real IOP changes using an external manometer connected to the anterior chamber and then to compare these changes when using two well-known methods, a mechanical keratome and low-pressure IntraLase technology, to perform LASIK.

From the [1]Vissum Hospital Oftalmológico, Madrid, Spain; [2]E. U. Óptica, Universidad Complutense de Madrid, Madrid, Spain; and [3]Hospital Universitario Príncipe de Asturias, Universidad de Alcalá, Madrid, Spain.

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Disclosure: **J.L. Hernández-Verdejo**, None; **M.A. Teus**, None; **J.M. Román**, None; **G. Bolívar**, None

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Investigative Ophthalmology & Visual Science, January 2007, Vol. 48, No. 1

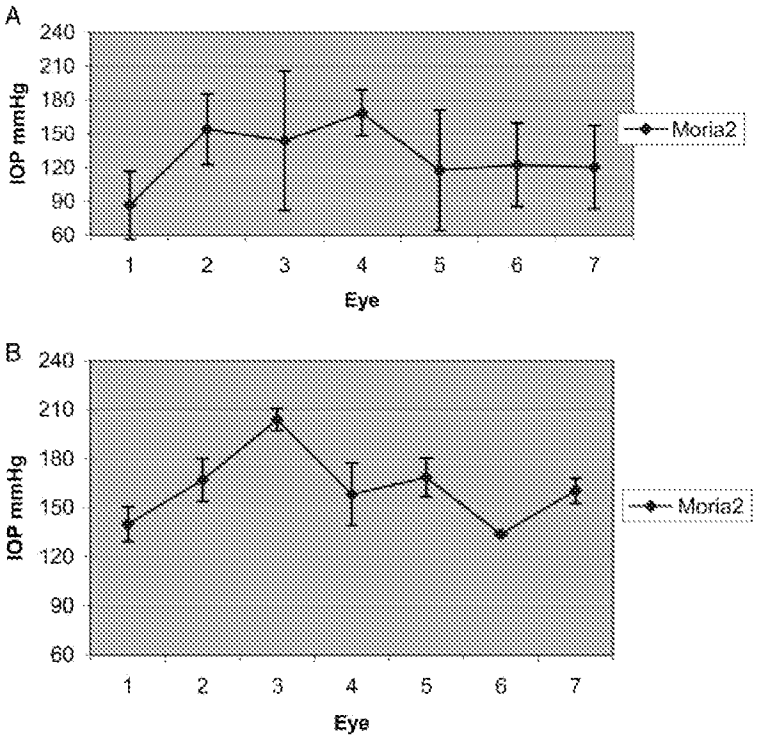

FIGURE 1. Mean IOP ± SD in each eye in the Moria group during the suctioning (A) and cutting (B) phases. IOPs were recorded every 5 seconds from the exact moment that the suction ring was applied. The mean time was 21.42 ± 7.48 seconds in the suctioning phase and 15.00 ± 2.88 seconds in the cutting phase.

MATERIALS AND METHODS

In this experimental model, using porcine eyes, we prospectively evaluated the changes in IOP from the application of the suction ring through the end of the passage of the mechanical microkeratome (M2; Moria, Antony, France) or creation of the nonmechanical flap with the femtosecond laser (IntraLase Corp., Irvine, CA).

Fourteen freshly enucleated porcine eyes were separated into two groups of seven eyes each: the Moria group and the IntraLase group. All eyes were free of corneal damage when inspected by slit lamp microscopy.

The eyes were inflated with a 5% glycosylated solution through the optic nerve (in the same manner described by Kasetsuwan et al.[9]) to obtain an IOP of 8 to 20 mm Hg checked with a Perkins applanation tonometer; the eyes were placed on a stand with sufficient support to withstand the surgical procedure. The IOP was measured in the anterior chamber using a 27-gauge winged infusion (Set REF 387412 Vialmset BD Biosciences, Hull, UK) that was inserted through the limbus in such a way that the suction ring could be applied over the sclera without touching the needle. Pressure measurements were obtained with a reusable blood pressure transducer (MLT0380 Reusable BP Transducer, Power Laboratory; AD Instruments, Racine, WI). The transducer is an external sensor for coupling to vascular pressure (in our experiment the IOP in the anterior chamber) via a liquid-filled catheter. A saline-filled silicone tube attached to the catheter was connected to the transducer. The transducer was prepared according to the instructions of the manufacturer, to assure a tight seal and that all air was flushed from the system. The recorder was set to 0 to initialize the transducer. Before starting the procedure, the transducer was checked to verify that the pressure would be registered correctly. For calibration, we connected the transducer to a mercury-calibrated column and then checked that the pressure in the mercury column and the display connected to the transducer were the same.

The suction ring was applied, and a flap was created in the eyes in both groups. The same experienced surgeon (JMR) performed all procedures on 1 day under direct microscopy visualization. During the procedure, the IOP was recorded continuously with the amplifier (ML110 Bridge Amplifier; AD Instruments, Castle Hill, Australia) connected to the barometric transducer, from the time of the application of the suction ring through the end of the microkeratome pass. IOP also was measured before and after the suction ring was placed, by using a Perkins handheld tonometer (Clement Clarke, Essex, UK). The IOP level after the procedure had to be at least 6 mm Hg, to rule out any substantial fluid leakage from the eye during the experiment.

Statistical analysis was performed using Student's *t*-test and the nonparametric Wilcoxon signed-rank test. $P < 0.05$ was considered significant.

RESULTS

Seven porcine eyes were studied in each group. In the Moria group, the mean IOP during suction was 122.52 ± 30.40 mm Hg (Fig. 1A) compared with 89.24 ± 24.26 mm Hg in the IntraLase group ($P = 0.001$). During flap creation, the mean IOP was 160.52 ± 22.73 mm Hg in the Moria group (Fig. 2A) compared with 119.33 ± 15.88 mm Hg in the IntraLase Group (Fig. 2B; $P = 0.001$).

The actual IOP immediately before suctioning was 11.5 ± 3.43 mm Hg ($r = 8$–16) in the IntraLase group and 17.28 ± 3.25 mm Hg ($r = 11$–20) in the Moria group. The IOP recorded by the transducer immediately after the maneuvers was 8.85 ±

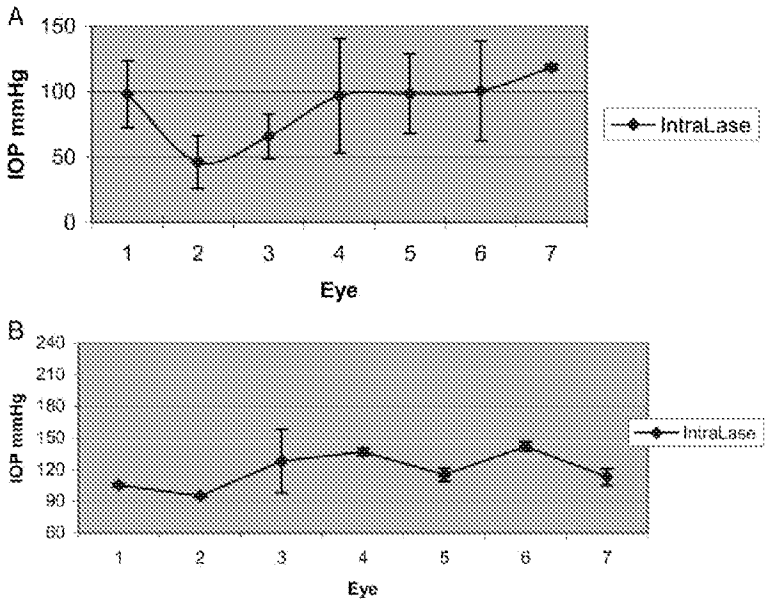

FIGURE 2. Mean IOP ± SD in each eye in the IntraLase group during the suctioning (A) and cutting (B) phases. The IOP was recorded every 5 seconds from the exact moment that the suction ring was applied. The mean time was 40 ± 9.57 seconds in the suctioning phase and 52.85 ± 5.66 seconds in the cutting phase.

2.11 mm Hg (r = 7 to 12) in the IntraLase group and 13.71 ± 3.63 mm Hg (r = 7 to 18) in the Moria group.

The mean time required to complete the suctioning was 21.42 ± 7.48 seconds (range, 15–35 seconds) in the Moria group compared with a mean of 40 ± 9.57 seconds (range, 30–55 seconds) in the IntraLase group (P = 0.04). The mean time needed to create the flap was 15.00 ± 2.88 seconds (range, 15 to 20 seconds) in the Moria group compared with 52.85 ± 5.66 seconds (range, 50 to 65 seconds) in the IntraLase group (P = 0.008; Fig. 3, Tables 1B, 2B).

The total time needed to complete the procedure in the Moria group was 36.42 ± 7.48 seconds and in the IntraLase group was 92.85 ± 13.49 seconds. The IntraLase procedure took twice as long as the mechanical procedure (P = 0.001).

DISCUSSION

In this animal model, we measured the real IOP in enucleated porcine eyes with two suction and cutting procedures during LASIK. Both groups had an IOP increase immediately after the placement of the suction ring that was maintained during the entire surgical procedure. We found differences both in suction time and in the real IOP levels that were achieved in both groups.

Bissen-Miyajima et al.[5] measured the IOP changes during LASIK using a direct method in porcine eyes. In that experiment, an intravenous pressure sensor was inserted into the vitreous cavity, whereas in our study the sensor was introduced into the anterior chamber. Despite this design difference, the study performed by those investigators showed a mean IOP increase of 99.1 ± 6.1 mm Hg, measured by a single-port suction ring and 99.0 ± 6.5 mm Hg using a dual-port suction ring during mechanical microkeratome use. In another study performed in human cadaveric eyes,[6] the measurements were obtained by entering the vitreous cavity through a pars plana incision. The results at two vacuum-pressure settings (488 and 600 mm Hg) after application of the suction ring alone were 93.3 ± 2.6 mm Hg for the 488-mm Hg

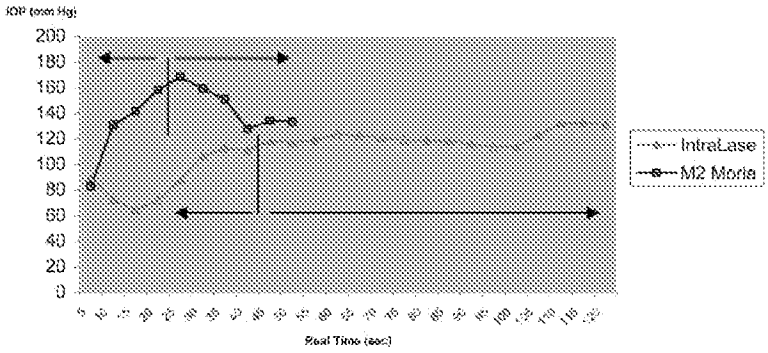

FIGURE 3. IOP increases in mm Hg over time, measured every 5 seconds, in both groups of seven eyes each, in the Moria mechanical microkeratome group and the IntraLase group. *Vertical lines*: the exact moment at which the cutting began. Suction time, 21.42 ± 7.48 seconds in the Moria group and 40 ± 9.57 seconds in the IntraLase group; cutting or flap time, 15.00 ± 2.88 seconds in the Moria group and 52.85 ± 5.66 seconds in the IntraLase Group.

TABLE 1. Moria Group

A. IOP Increases in IOP in Each Eye from Application of the Suction Ring to the End of Flap Creation

Eye	Mean (mm Hg)	SD	Range
1	106.5	±36.39	40–148
2	160.5	±22.66	120–182
3	173.83	±51.52	72–208
4	161.67	±21.52	127–182
5	140.75	±52.94	60–219
6	125.8	±30.61	47–147
7	131.71	±36.09	62–166

B. IOPs Recorded during the Study

Eye	IOP Pre	IOP Suction	IOP Cut	IOP Post	Suction Time (s)*	Cutting Time (s)*
1	15	86.4	140	11	25	15
2	20	154	167	14	15	15
3	20	89	204	16	15	15
4	18	168.3	155	15	15	15
5	11	117.5	164	7	20	20
6	18	122.28	134	15	35	15
7	19	120.2	159.66	18	25	10
Mean	17.28	122.52	160.52	13.71	21.42	15
SD	3.25	30.4	22.73	3.63	7.48	2.88

Initial IOP (IOP pre), mean IOP (in mm Hg) of the suctioning phase (IOP Suction), mean IOP of the cutting phase (IOP Cut), and final IOP (IOP Post) immediately after the cutting phase for each of the seven eyes.

* The two columns on the right show the suctioning and cutting time for each eye expressed as the mean ± SD.

group and 108.0 ± 22.1 mm Hg for the 600-mm Hg group; during the microkeratome pass, the mean IOP was 82.0 ± 15.0 mm Hg for the 488-mm Hg group and 92.5 ± 38.8 mm Hg for the 600-mm Hg group. The pressure changes during the microkeratome pass were not statistically significant. The lower levels of IOP found in those two studies may reflect the fact that the velocity at which the pressure is transmitted in a fluid-filled tube depends on the fluid viscosity, and it therefore seems reasonable to consider that the measurements registered through the anterior chamber, as in the present study, should be more precise than those obtained through the vitreous chamber.

In our study, the IOP increased in both groups, although it followed a different pattern. For example, in the Moria group, the mean IOP increase during suctioning was 122.53 ± 30.40 mm Hg and reached a mean 160.52 ± 22.73 mm Hg during the creation of the lamellar corneal flap. We also observed a great deal of fluctuation in the IOP levels. However, in the IntraLase group, the mean IOP during suctioning was 89.24 ± 24.57 and 119.0 ± 17.01 mm Hg during the flap creation. In this case, the

TABLE 2. IntraLase Group

A. IOP Increases in IOP in Each Eye from Application of the Suction Ring to the End of Flap Creation

Eye	Mean (mm Hg)	SD	Range
1	101.75	±18.02	(59–129)
2	76.69	±35.72	(34–114)
3	99.54	±33.84	(36–132)
4	109.06	±35	(45–160)
5	107.72	±21.54	(70–141)
6	127.35	±30.1	(72–157)
7	115.35	±3.18	(112–122)

B. IOPs Recorded during the Study

Eye	IOP Pre	IOP Suction	IOP Cut	IOP Post	Suction Time (s)*	Cut Time (s)*
1	13	98.2	105.3	11	50	50
2	9	46.16	95	9	30	50
3	8	65.72	128.15	6	55	65
4	8	96.87	136.8	7	40	50
5	15	98.5	115.1	9	40	50
6	16	100.66	141.9	12	30	55
7	9	118.57	113.1	8	35	50
Mean	11.5	89.24	119.33	8.85	40	52.85
SD	3.43	24.26	15.88	2.11	9.57	5.66

The initial IOP (in mm Hg; IOP Pre), mean IOP of the suctioning phase (IOP Suction), mean IOP of the cutting phase (IOP Cut), and the final IOP (IOP Post) immediately after the cutting phase for the seven eyes.

* The two columns to the right show the suctioning and cutting time for each eye expressed as the mean and standard deviation.

IOP increase was more stable throughout the procedure, especially during the cutting of the flap.

Previous studies have reported that the LASIK flap may induce higher-order aberrations (HOAs) and advocate the use of photorefractive keratectomy for wavefront-guided treatments.[20] Recently, Durrie and Kezirian[21] reported that the IntraLase femtosecond laser induces fewer HOAs, less residual spherical equivalent, and less residual astigmatism, and has better predictability than does photorefractive keratectomy. Kasetsuwan et al.[6] showed that the pressure setting for the suction ring is an important variable in determining consistent corneal flap thickness during LASIK. An interesting aspect of our study was that the IOP levels achieved during the IntraLase procedure were lower and more stable than those achieved when creating a flap with a mechanical microkeratome.

Sudden increases in IOP, although well tolerated, may induce changes in the peripheral retina, as described by Charteris et al.,[10] Krueger et al.,[14] and Flaxel et al.[13] These possible posterior segment complications, among others, make the knowledge of the exact IOP increase induced by surgical procedures such as laser refractive surgery increasingly important.

In our experiment, the IntraLase group had lower IOP increases, although the time needed for the surgical maneuver was almost twice that of the Moria group. It would be interesting to determine which of these factors is more reliable for ocular safety, the time for which the eye is subjected to increased IOP levels or simply the level of the IOP.

There are limitations when using enucleated porcine eyes, because the corneas, although freshly enucleated, were slightly edematous and because the IOP was achieved by an infusion of a glycosylated solution. Clearly, further research is needed in this field.

Real-time IOP can be measured during LASIK with a transducer connected to the anterior chamber. Our results showed a significant increase in IOP during the procedure in both groups, although IntraLase seems to increase the IOP to a significantly lesser extent than does the conventional mechanical microkeratome.

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EVIDENCE - 4

Ultrasound Biomicroscopic Findings in Rabbit Eyes Undergoing Scleral Suction during Lamellar Refractive Surgery

Wei-Li Chen, Yung-Feng Shih, Shu-Lang Liao, Fung-Rong Hu, and Por-Tying Hung

Purpose. To evaluate changes of the central anterior chamber depth, cilio-angular cross-sectional surface area, and intraocular pressure in rabbit eyes undergoing application of the scleral suction ring during lamellar refractive surgery.

Methods. Thirty eyes of 30 rabbits were used in the study. The eyes were assigned to one of the following five surgical groups: group 1, no application of the suction ring; group 2, suction for 2 minutes; group 3, suction for 1 minute; group 4, suction for 20 seconds; and group 5, suction for 10 seconds. Ultrasound biomicroscopy (UBM) was performed to determine tomographic features, including central anterior chamber depth, cross-sectional surface area of the ciliary body, and chamber angle structure before and 10 minutes, 1 hour, 2 hours, 1 day, 2 days, 1 week, and 2 weeks after surgery. Intraocular pressure was also measured at each of these time points.

Results. Swelling of the ciliary body occurred in groups 2 to 5 of eyes from 10 minutes up to 1 day after the operation, and its severity was positively related to the duration of suction. Shallowness of the chamber angle was positively related to swelling. All UBM-detectable changes became insignificant compared with baseline values at 2 days after the operation. No significant change was found in the central anterior chamber depth and intraocular pressure during the 2-week postoperative observation period.

Conclusions. Transient change in the ciliary body and the chamber angle occurred frequently after application of the scleral suction ring during lamellar refractive surgery in rabbit eyes. Its severity was positively related to the duration of suction. Swelling of the ciliary body corresponded with the shallowness of the chamber angle without alteration of the corneal–lenticular distance and intraocular pressure. (*Invest Ophthalmol Vis Sci.* 2002;43:3665–3672)

Changes in the ciliary body and angle of the anterior chamber, such as ciliary detachment or angle closure, occasionally occur after surgery for retinal detachment or cataract, pars plana vitrectomy, and filtering surgery. These changes may also occur in eyes of patients who have hypotony, uveitis, concussion injury, or phthisis bulbi.[1–5] However, the likelihood of the occurrence of these changes after lamellar refractive surgery is not well established.

The ciliary body, extending anteriorly from the anterior choroids and peripherally to the iris, is anatomically situated under the covering area of the suction ring used in lamellar refractive surgery. It is reasonable to suspect that transient or permanent damage to the underlying structures may occur after application of the suction ring. In this study, we used ultrasound biomicroscopy (UBM) to perform preoperative and postoperative examinations focusing on central anterior chamber depth (CACD), cross-sectional surface area of the ciliary body (CBCSA), and the chamber angle in rabbit eyes undergoing application of the suction ring with different durations of suction. The purpose of this study was to determine whether the mechanical force exerted by application of the scleral suction ring damages the ciliary body or other associated structures in rabbit eyes and also to evaluate the effects of different durations of suction.

Material and Methods

All experimental procedures were performed in accordance with the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research. Right eyes of 30 adult male New Zealand White rabbits, weighing 3.5 to 4 kg, underwent surgery and were examined. Surgery and examinations were performed with rabbits under general anesthesia with intramuscular injection of 35 mg/kg ketamine HCl and 5 mg/kg xylazine (Rompun; Bayer Sverige AB, Uppsala, Sweden). Thirty eyes were equally divided into five groups with different durations of suction. In group 1, the eyes were mildly proptosed for 2 minutes without application of the suction ring (control group). Suction was performed in group 2 for 2 minutes, group 3 for 1 minute, group 4 for 20 seconds, and group 5 for 10 seconds. After lateral canthotomy was performed, a suction ring of the manual microkeratome (SCMD; United Development Corp., Fountain Hills, AZ) was placed at the sclerocorneal plane of the gently proptosed eye and carefully centered. The suction ring was then firmly applied to the globe. Good adherence to the globe was ensured by observing a small displacement and the slight mydriasis induced by the suction itself. During the suction period, tonometry was performed with a Barraquer tonometer. An intraocular pressure (IOP) of at least 65 mm Hg was confirmed during the whole period of surgery. UBM examinations were made before surgery and at 10 minutes, 1 hour, 2 hours, 1 day, 2 days, 1 week, and 2 weeks after surgery. At each preoperative and postoperative time point, the IOP was measured with a handheld tonometer (TonoPen; Mentor, Norwell, MA).

Ultrasound Biomicroscopy

UBM examinations were performed with a commercial version of the ultrasound biomicroscope (Humphrey Instruments, San Leandro, CA), with a 50-MHz transducer-probe allowing 4- to 5-mm tissue penetration and approximately 50-μm resolution, and a 1.5% hydroxyethylcellulose-filled eye cup. Each eye was examined in its axial section, exploring the transverse diameter passing through the apex of the cornea from the 3-o'clock to the 9-o'clock position (temporal sector) in constant ambient lighting conditions (illumination: 190 lux). Fine move-

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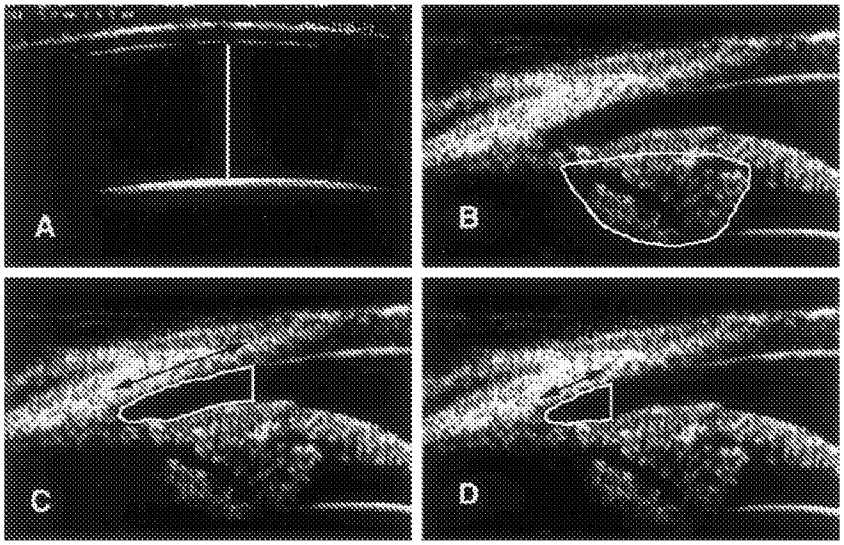

FIGURE 1. Morphologic parameters associated with UBM images. (A) Anterior chamber; *line*: anterior chamber depth. (B) Ciliary process; *line*: outline of the CBCSA. (C) ASA-2000; *line*: outline of the cross-sectional surface area of ASA-2000; *double arrow*: 2000-μm width. (D) ASA-1000; *line*: outline of the cross-sectional surface area of ASA-1000; *double arrow*: 1000-μm width.

ments of the probe were also performed to explore the areas of interest perpendicularly at the temporal area. Images of three areas of interest, including centered on the pupil, the temporal angular region, and the temporal ciliary process, were frozen. Four sets of scans of these areas of interest were obtained. The various anterior segment parameters, described in the following section, were measured on these images with a special caliper issued with the instrument's software package and manipulated by the examiner.

Morphologic Parameters

The definitions of the morphologic parameters assessed were modified from previous studies as follows[6–9]:

1. Central anterior chamber depth (CACD): measured as the central corneal endothelium to the central anterior lens surface (Fig. 1A).
2. Ciliary body cross-sectional surface area (CBCSA): measured as the cross-sectional surface area of the ciliary body with the plane along the longest part of the ciliary process. The ciliary processes were manually selected and isolated (Fig. 1B).
3. Angular surface area 2000 (ASA-2000): the cross-sectional surface area encompassed by the posterior corneal surface, anterior iris surface, and a straight line passing through a point on the posterior corneal surface at 2000 μm from the scleral spur and the point on the anterior iris surface perpendicularly opposite (Fig. 1C).
4. Angular surface area 1000 (ASA-1000): the cross-sectional surface area encompassed by the posterior corneal surface, anterior iris surface, and a straight line passing through a point on the posterior corneal surface at 1000 μm from the scleral spur and the point on the anterior iris surface perpendicularly opposite (Fig. 1D).
5. The presence of ciliary detachment.

In the measurement of parameters 2 to 4, the region of the ciliary body and angular surface area were manually delineated, and quantitative analyses of the images were performed by a single individual blinded to the treatment conditions. With computer planimetry, the border of each image was traced three times, and the automatically measured surface areas were averaged. Measurements of linear parameters were expressed in millimeters and surface area parameters in square millimeters.

Statistical Analysis

In every surgical condition, four sets of UBM images in each eye were scanned, and three calculations were made in each image. The average result of 12 measurements in each eye were calculated. Data are expressed as the mean ± SD. Reproducibility of each eye in each condition was measured by averaging the proportional relationship of the standard deviation of the repeated 12 measures to the mean of those measures. (i.e., coefficient of variation [CV]). Reproducibility of parameters 1 to 4 was measured by average of the CV of the 30 eyes at eight time points. (five groups, each group contains six eyes, each eye had one preoperative and seven postoperative measurements). A CV less than 10% was considered indicative of good reproducibility. The mean of each of the postoperative measurements was compared with the preoperative data, using a paired, two-tailed Student's *t*-test. Pearson's correlation test was used to evaluate the correlation between the change in CBCSA with the change in ASA-2000, ASA-1000, and CACD. $P < 0.05$ was considered to indicate statistical significance.

RESULTS

The CVs of the parameters CACD, CBCSA, ASA-2000, and ASA-1000 were 2.89 ± 0.09, 5.43 ± 0.21, 6.84 ± 0.45, and 7.15 ± 0.52, respectively. The reproducibility of these four parameters was high (CV ≤ 10%).

Figure 2 represents the ciliary body and change in chamber angle surface area after continuous suction for 2 minutes in one rabbit eye in group 2. In these images, we can easily see the increase in CBCSA and decrease in angular surface area 10 minutes and 1 hour after surgery. In the image at 10 minutes after surgery, near total occlusion of the peripheral angle and iridocorneal touch in the midperipheral iris were seen. These changes became less significant 1 day after surgery.

Ciliary Body Cross-sectional Surface Area

Table 1 summarizes the results of preoperative and postoperative CBCSA. There was no significant change in CBCSA in the control group (group 1). The CBCSAs in groups 2 to 5 were increased after surgery at 10 minutes, 1 hour, and 2 hours. The CBCSA decreased 1 day after surgery in all four groups. However, it was still higher than preoperative measurements in all groups. The significance of the postoperative increase in

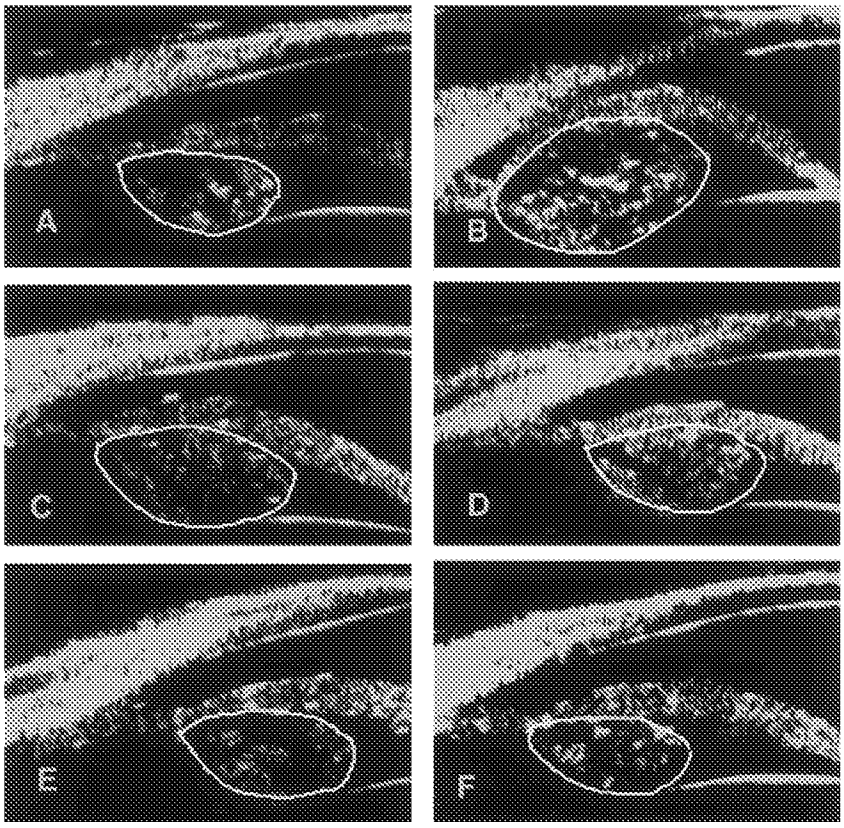

FIGURE 2. UBM image of ciliary body and chamber angle surface area changes in one rabbit eye (eye 2, as shown in Fig. 3) undergoing suction ring application for 2 minutes. (A) Before surgery, (B) 10 minutes after surgery, (C) 1 hour after surgery, (D) 1 day after surgery, (E) 2 days after surgery, and (F) 2 weeks after surgery. *Line*: CBCSA.

CBCSA disappeared 2 days after the operation in all groups. We also noted the positive relationship between the duration of suction and the increase in CBCSA. (Table 1). Group 2 had the largest increase in CBCSA, followed by groups 3 and 4. Group 5 had the smallest increase at each time point. Figure 3 summarizes the time sequence changes in CBCSA in eyes undergoing scleral suction for 2 minutes in group 2.

ASA-2000 and ASA-1000

Table 2 summarizes the changes in ASA-2000 and ASA-1000 in the UBM study. There were no significant changes in ASA-2000 and ASA-1000 in the control group (group 1). There was a significant decrease in ASA-2000 compared with preoperative values in groups 2 to 5 at 10 minutes, 1 hour, and 2 hours after surgery. A decrease was also found in ASA-1000 in groups 2 to 5 at 10 minutes, 1 hour, and 2 hours after surgery. This significance was not found at 2 days after surgery in any surgical group. We also noted the positive relationship between duration of suction and decrease in ASA-2000 and ASA-1000. Group 2 had the largest decrease in ASA-2000 and ASA-1000, followed by groups 3 and 4. Group 5 had the smallest decrease in ASA-2000 and ASA-1000 at each time point. Figure

TABLE 1. Preoperative and Postoperative Ciliary Body Cross-Sectional Surface Area

	Group 1 (Control)		Group 2 (Suction for 2 Minutes)		Group 3 (Suction for 1 Minute)		Group 4 (Suction for 20 Seconds)		Group 5 (Suction for 10 Seconds)	
	Mean ± SD	*P*	Mean ± SD	*P*	Mean ± SD	*P*	Mean ± SD	*P*	Mean ± SD	*P*
Preoperative	1.52 ± 0.09		1.53 ± 0.10		1.60 ± 0.08		1.46 ± 0.10		1.51 ± 0.07	
Postoperative										
10 minutes	1.51 ± 0.05	NS	2.14 ± 0.21	0.007	2.12 ± 0.15	0.013	1.69 ± 0.05	0.019	1.65 ± 0.07	0.047
1 hour	1.49 ± 0.07	NS	2.13 ± 0.16	0.011	1.95 ± 0.18	0.026	1.69 ± 0.05	0.018	1.64 ± 0.03	0.045
2 hours	1.53 ± 0.04	NS	2.07 ± 0.21	0.016	2.01 ± 0.09	0.023	1.72 ± 0.11	0.028	1.54 ± 0.10	NS
1 day	1.50 ± 0.08	NS	1.68 ± 0.09	0.026	1.72 ± 0.13	0.039	1.66 ± 0.13	0.042	1.53 ± 0.06	NS
2 days	1.52 ± 0.11	NS	1.62 ± 0.10	NS	1.68 ± 0.07	NS	1.54 ± 0.11	NS	1.52 ± 0.12	NS
1 week	1.53 ± 0.13	NS	1.61 ± 0.08	NS	1.64 ± 0.11	NS	1.44 ± 0.12	NS	1.50 ± 0.04	NS
2 weeks	1.51 ± 0.06	NS	1.54 ± 0.11	NS	1.57 ± 0.08	NS	1.46 ± 0.10	NS	1.49 ± 0.08	NS

The mean value in square millimeters of each of the postoperative parameters was compared with the preoperative data, by paired, two-tailed Student's *t*-test. $P < 0.05$ was considered to indicate statistical significance. NS, not significant.

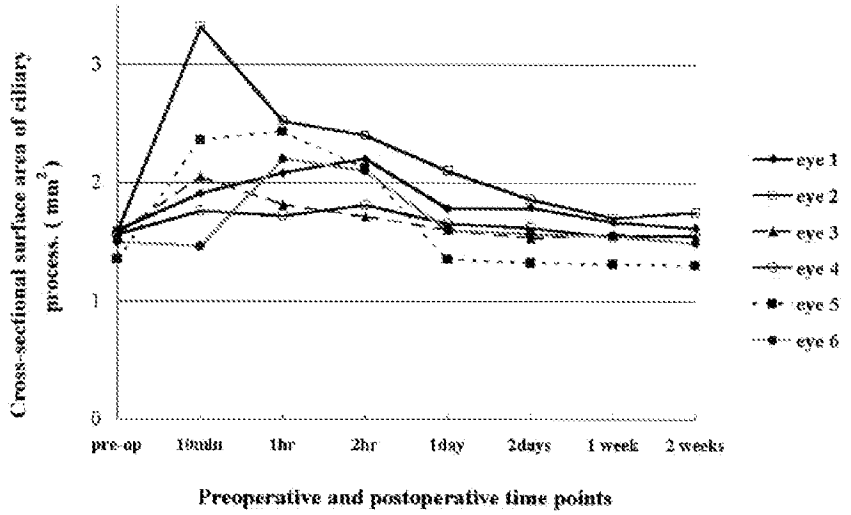

FIGURE 3. Change in CBCSA in six rabbit eyes in group 2 at each postoperative time point, after surgery involving a 2-minute application of the suction ring.

4 summarizes the time sequence changes of ASA-1000 in eyes undergoing scleral suction for 2 minutes in group 2.

Central Anterior Chamber Depth

Table 3 summarizes the CACD measured in the UBM study. The preoperative CACD ranged from 2.29 to 2.38 mm. No significant change in CACD compared with preoperative data was found at any of the postoperative time points in all five groups.

Correlation of the Increase in CBCSA with the Decrease of ASA-2000, ASA-1000, and CACD

The correlation of the increase in CBCSA and the decrease in ASA-2000 was 0.917 ($P < 0.001$), the correlation of the increase in CBCSA and the decrease in ASA-1000 was 0.892 ($P < 0.001$), and the correlation of the increase in CBCSA and CACD was 0.129 ($P = 0.512$).

Presence of Ciliary or Anterior Choroidal Detachment

No ciliary or anterior choroidal detachment was found in any of the experimental rabbit eyes at any time point after surgery.

Changes in IOP

Table 4 summarizes the results of IOP measurements. The preoperative IOP ranged from 9.6 to 12.3 mm Hg. No significant change was found in IOP compared with preoperative data at any of the postoperative time points in all five groups.

TABLE 2. Preoperative and Postoperative ASA-2000 and ASA-1000

	Group 1 (Control)		Group 2 (Suction for 2 minutes)		Group 3 (Suction for 1 minute)		Group 4 (Suction for 20 seconds)		Group 5 (Suction for 10 seconds)	
	Mean ± SD	*P*	Mean ± SD	*P*	Mean ± SD	*P*	Mean ± SD	*P*	Mean ± SD	*P*
ASA-2000										
Preoperative	0.70 ± 0.05		0.75 ± 0.02		0.78 ± 0.06		0.69 ± 0.04		0.74 ± 0.04	
Postoperative										
10 minutes	0.71 ± 0.04	NS	0.49 ± 0.08	<0.001	0.55 ± 0.08	0.001	0.56 ± 0.07	0.008	0.61 ± 0.05	0.024
1 hour	0.72 ± 0.13	NS	0.48 ± 0.11	<0.001	0.61 ± 0.09	0.002	0.56 ± 0.07	0.011	0.59 ± 0.13	0.017
2 hours	0.68 ± 0.09	NS	0.56 ± 0.09	0.009	0.65 ± 0.06	0.007	0.62 ± 0.07	0.032	0.57 ± 0.09	0.021
1 day	0.72 ± 0.11	NS	0.68 ± 0.05	0.018	0.71 ± 0.05	0.013	0.63 ± 004	0.034	0.69 ± 0.11	NS
2 days	0.69 ± 0.14	NS	0.72 ± 0.03	NS	0.76 ± 0.06	NS	0.66 ± 0.07	NS	0.68 ± 0.13	NS
1 week	0.71 ± 0.12	NS	0.74 ± 0.02	NS	0.77 ± 0.07	NS	0.67 ± 0.05	NS	0.71 ± 0.12	NS
2 weeks	0.70 ± 0.07	NS	0.75 ± 0.03	NS	0.79 ± 0.06	NS	0.68 ± 003	NS	0.73 ± 0.11	NS
ASA-1000										
Preoperative	0.32 ± 0.05		0.31 ± 0.03		0.33 ± 0.04		0.30 ± 0.02		0.32 ± 0.03	
Postoperative										
10 minutes	0.31 ± 0.04	NS	0.21 ± 0.01	<0.001	0.23 ± 0.02	<0.001	0.22 ± 0.04	0.001	0.25 ± 0.02	0.007
1 hour	0.30 ± 0.09	NS	0.20 ± 0.02	<0.001	0.23 ± 0.02	<0.001	0.24 ± 0.01	0.008	0.26 ± 0.01	0.012
2 hours	0.32 ± 0.06	NS	0.21 ± 0.03	<0.001	0.25 ± 0.03	<0.001	0.24 ± 0.03	0.017	0.27 ± 0.03	0.037
1 day	0.32 ± 0.11	NS	0.27 ± 0.03	0.026	0.31 ± 0.03	0.033	0.25 ± 0.03	0.032	0.30 ± 0.01	NS
2 days	0.31 ± 0.07	NS	0.28 ± 0.04	NS	0.33 ± 0.04	NS	0.26 ± 0.02	NS	0.31 ± 0.05	NS
1 week	0.30 ± 0.08	NS	0.30 ± 0.02	NS	0.32 ± 0.02	NS	0.29 ± 0.03	NS	0.33 ± 0.07	NS
2 weeks	0.32 ± 0.07	NS	0.31 ± 0.03	NS	0.33 ± 0.04	NS	0.30 ± 0.02	NS	0.32 ± 0.06	NS

Data are expressed as in Table 1.

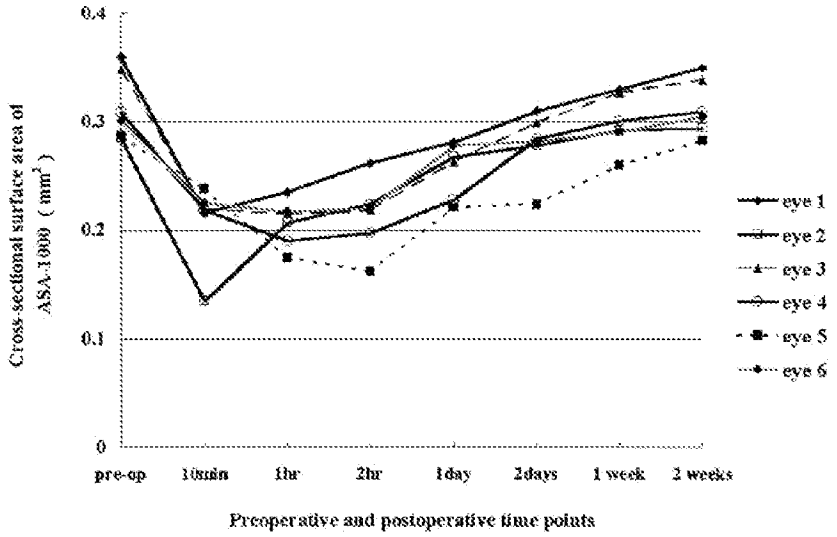

FIGURE 4. Change in ASA-1000 in six rabbit eyes in group 2 at each of the postoperative time points, after surgery involving a 2-minute application of the suction ring.

DISCUSSION

LASIK, one of the various types of lamellar refractive surgery, has gained in popularity worldwide over recent years for the correction of myopia, hyperopia, and astigmatism, because of its excellent surgical results and relatively low complication rate.[10–12] However, some adverse effects, such as flap-related problems, epithelium-associated problems, diffuse lamellar keratitis, and infectious keratitis still occur.[13–17] Suction ring–related complications, such as inadequate suction or total loss of suction, are another potential source of serious problems during LASIK. Other possible suction ring–related complications include retinal vascular occlusion, ischemic optic neuropathy, or macular hemorrhage due to elevation of OP during surgery.[18–20] To perform a perfect lamellar cut with the microkeratome, the IOP must be increased to an adequate level for an adequate duration. Experimental animal studies have found that IOP can increase to between 80 and 230 mm Hg during the vacuuming phase and even greater pressures, from 140 to 360 mm Hg, can occur during the lamellar cut.[21–22] Theoretically, a prolonged high IOP would cause retinal vascular occlusion, especially in patients with vasculopathies or diabetes. Subconjunctival hemorrhage caused by the pneumatic suction ring is another complication mostly without sequelae.[23] It occurs commonly with prolonged suction, excessive eye manipulation, or treatment with platelet-modifying agents such as aspirin or other antiarthritic medications. Another theoretically possible complication is damage to the ciliochoroid and associated structures caused by suction ring–related vacuum pressure. A presumed ciliary body shutdown, with delayed severe hypotony and the presence of nonrhegmatogenous retinal detachment in a patient with keratomileusis was recently reported.[24] However, large series studies on the ciliary body changes after lamellar refractive surgery have not been reported.

Ciliochoroidal changes, such as ciliary body swelling, shallowing of chamber angle or ciliochoroidal detachment have been occasionally noted after intraocular surgery.[1–5] The ciliary body is more susceptible to detachment or other mechanical damage than other parts of the uveal tissue, because no attachment is present between the longitudinal ciliary muscles and the sclera from the scleral spur to the epichoroidal stars in the pars plana.[1] Surgery induced ciliochoroidal detachment is usually temporary and does not cause permanent complications.[1,2,5] However, postoperative thickening of the ciliary

TABLE 3. Preoperative and Postoperative Central Anterior Chamber Depth

	Group 1 (Control)		Group 2 (Suction for 2 Minutes)		Group 3 (Suction for 1 Minute)		Group 4 (Suction for 20 Seconds)		Group 5 (Suction for 10 Seconds)	
	Mean ± SD	P	Mean ± SD	P	Mean ± SD	P	Mean ± SD	P	Mean ± SD	P
Preoperative	2.37 ± 0.01		2.29 ± 0.01		2.31 ± 0.02		2.38 ± 0.03		2.35 ± 0.03	
Postoperative										
10 minutes	2.36 ± 0.02	NS	2.28 ± 0.01	NS	2.31 ± 0.02	NS	2.37 ± 0.02	NS	2.34 ± 0.02	NS
1 hour	2.37 ± 0.01	NS	2.28 ± 0.02	NS	2.30 ± 0.04	NS	2.36 ± 0.03	NS	2.35 ± 0.04	NS
2 hours	2.35 ± 0.01	NS	2.29 ± 0.03	NS	2.31 ± 0.01	NS	2.38 ± 0.01	NS	2.35 ± 0.02	NS
1 day	2.37 ± 0.02	NS	2.30 ± 0.02	NS	2.29 ± 0.03	NS	2.37 ± 0.02	NS	2.36 ± 0.03	NS
2 days	2.38 ± 0.01	NS	2.31 ± 0.02	NS	2.32 ± 0.01	NS	2.36 ± 0.01	NS	2.35 ± 0.01	NS
1 week	2.36 ± 0.04	NS	2.30 ± 0.01	NS	2.31 ± 0.02	NS	2.37 ± 0.05	NS	2.34 ± 0.02	NS
2 weeks	2.38 ± 0.01	NS	2.28 ± 0.03	NS	2.29 ± 0.01	NS	2.39 ± 0.04	NS	2.36 ± 0.03	NS

The mean value in millimeters of each of the postoperative parameters was compared with the preoperative data, by paired, two-tailed Student's *t*-test. $P < 0.05$ was considered to indicate statistical significance. NS, not significant.

TABLE 4. Preoperative and Postoperative IOP

	Group 1 (Control)		Group 2 (Suction for 2 Minutes)		Group 3 (Suction for 1 Minute)		Group 4 (Suction for 20 Seconds)		Group 5 (Suction for 10 Seconds)	
	Mean ± SD	*P*	Mean ± SD	*P*	Mean ± SD	*P*	Mean ± SD	*P*	Mean ± SD	*P*
Preoperative	11.37 ± 0.21		12.29 ± 0.11		10.51 ± 0.22		9.68 ± 0.03		12.15 ± 0.23	
Postoperative										
10 minutes	11.16 ± 0.15	NS	12.38 ± 0.41	NS	11.01 ± 0.42	NS	9.77 ± 0.06	NS	11.94 ± 0.32	NS
1 hour	11.87 ± 0.11	NS	12.09 ± 0.02	NS	10.80 ± 0.16	NS	9.76 ± 0.27	NS	12.05 ± 0.14	NS
2 hours	11.95 ± 0.18	NS	12.36 ± 0.13	NS	10.91 ± 0.49	NS	9.97 ± 0.31	NS	11.85 ± 0.62	NS
1 day	12.07 ± 0.22	NS	11.93 ± 0.22	NS	11.10 ± 0.23	NS	10.37 ± 0.22	NS	12.26 ± 0.23	NS
2 days	11.68 ± 0.31	NS	12.31 ± 0.17	NS	10.82 ± 0.51	NS	9.96 ± 0.53	NS	12.05 ± 0.51	NS
1 week	12.06 ± 0.42	NS	12.19 ± 0.41	NS	11.11 ± 0.42	NS	10.27 ± 0.05	NS	11.84 ± 0.72	NS
2 weeks	11.78 ± 0.16	NS	12.08 ± 0.23	NS	10.89 ± 0.21	NS	9.79 ± 0.06	NS	12.06 ± 0.17	NS

The mean value (in mm Hg) of each of the postoperative parameters was compared with the preoperative data, by paired, two-tailed Student's *t*-test. $P < 0.05$ was considered to indicate statistical significance. NS, not significant.

body may rotate the ciliary body anteriorly and cause angle closure.[25] Minamoto et al.[26] described a case of persistent hypotony after an otherwise successful vitreous surgery for epiretinal membrane, in which ciliochoroidal detachment was detected by UBM. Araie et al.[27] also suggested that postoperative ciliary body changes might result in reduction in formation of aqueous humor, which causes development of postoperative hypotony. Because the suction ring used in LASIK is positioned circumferentially from the limbus to approximately 3 mm away from it to the anterior sclera, which covers the anatomic portion of the ciliary body and the anterior choroid, it is reasonable to suspect that the mechanical force and the dramatic changes in IOP during and after use of the suction ring may damage the ciliochoroid and associated tissues.

Clinically apparent choroidal detachment can be checked with a funduscope or echography. However, with the anatomic position of the ciliary body concealed beneath the light-blocking iris and peripheral to the ora serrata, subtle swelling or detachment of the ciliary body remains difficult to evaluate in vivo. The recent development of the high-frequency UBM (Humphrey Instruments) has enabled observation of the chamber angle and ciliary body region at a high resolution that is unparalleled in traditional ophthalmic ultrasonographic instruments.[1,25,26] Methods of measuring the anterior segment parameters have been described. Pavlin et al.[6,7] defined several different anterior segment parameters that have been assessed with the aid of a caliper provided in the computer software accompanying the UBM.[9,29–32] However, due to the more prominent, more convoluted, and larger volume of the ciliary process in rabbit eyes than in human eyes,[33] these parameters are not useful in detecting anterior segment change in rabbit eyes. In this study, we developed a convenient method for measuring anterior segment parameters. The CBCSA and anterior chamber angle at different distances from the scleral spur may provide more convincing information about thickness of the ciliary process or angle opening than traditional one-dimensional measurements.[29,34] However, reproducibility can be a major problem in measuring anterior segment structure with the UBM. When we measure CBCSA, significant variation in cross-sectional area can be expected from plane to plane, depending on whether the plane was oriented along or between the ciliary process. In this study, the measuring plane was oriented along the longest part of the ciliary process determined by one individual who was blinded to the treatment condition. The high reproducibility in our study (CV < 10%) was consistent with the previous study which highlight the high intraobserver reproducibility in measuring UBM images.[35] High reproducibility was shown in the current study, not only of CBCSA, but of CACD, ASA-2000, and ASA-1000.

Ciliary detachment did not occur in any of our studied eyes, even in eyes receiving suction for 2 minutes, which was conceived to be the maximal tolerable suction duration during LASIK.[36] However, swelling of the ciliary body and shallowing of the chamber angle were found in all surgical groups. Longer suction duration led to more severe swelling in the ciliary body, and the swelling correlated positively with shallowing of the chamber angle. In a rabbit eye imaged 10 minutes after surgery involving use of the suction ring for 2 minutes, near total occlusion of the peripheral angle and iridocorneal touch in the midperipheral iris was noted (Fig. 2B). One explanation of these changes was swelling of the ciliary body, although it is also possible that pressure differences between the anterior and posterior chamber during suction may have led to bowing of the iris, which secondarily led to such a manifestation. The mechanism of suction ring–related swelling of the ciliary body is likely to be the uveal congestion from venous obstruction due to high IOP during the procedure, although the position of the scleral ring was not directly over or anterior to the vortex vein, as in case of scleral buckling.[34] It is also possible that local inflammation caused by the surgical procedure or the mechanical outward force exerted on the perilimbal sclera induced the swelling of the underlying ciliary body.

Several studies have reported on the correlation of anterior chamber depth with ciliary body thickness and chamber angle. Gohdo et al.[29] demonstrated that in human eyes with narrow chamber angle, thinning of the ciliary body may be a major factor associated with the anterior location of the lens, increased lens thickness, and decreased anterior chamber depth. Kobayashi et al.[31] showed a strong correlation among anterior chamber depth, trabecular–iris angle, and chamber angle opening in normal infants and children. However, Martinez-Bello et al.[30] showed that trabeculectomy alone widens the angle but does not affect the anterior chamber depth. Our results also showed that narrowing of the chamber angle did not significantly affect the CACD. That there was no change in IOP after surgery in this study is not surprising. The observed changes in ciliary body morphology do not necessarily imply impairment of its function. Also, although narrowed, the chamber angle was always at least partially open. One other less plausible explanation is that a transient decrease in aqueous humor production caused by ciliary body swelling and dysfunction could be compensated by the effect of angle shallowing, which results in partial obstruction of the outflow of aqueous humor and return of IOP.

Except for the possible effects on CACD and IOP, the ciliary body changes may also lead to accommodative impairment. The accommodative apparatus is driven principally by parasympathetic innervation of the ciliary smooth muscle and may cause a reduction in the diameter of the ciliary muscle collar that instigates a series of events leading to an ability to see near objects clearly.[37] In human eyes, the ciliary muscle, which resides in the stroma of the ciliary body, is attached anteriorly to the scleral spur by means of tendons and trabecular meshwork and posteriorly to the elastic network of Bruch's membrane in the choroid. There are no direct connections between the zonules and the ciliary muscle.[38] Therefore, the stroma of the ciliary body is responsible for the transduction of the force of ciliary muscle contraction to the zonules and may influence accommodation.[39] Because the rabbit eye is virtually nonaccommodative, we did not look at changes in accommodation in this study. Although there are no data on accommodation in human or rabbit eyes undergoing scleral suction during lamellar refractive surgery, it is possible that the ciliary body changes shown in our study influenced the function of ciliary muscle contraction, and thus impaired the accommodative ability. This may partially explain the mechanisms of transient accommodative impairment reported by some patients who undergo lamellar refractive surgery. Although a fundamental problem in studying accommodation in the human eye remains that essential structures of the accommodative apparatus are hidden behind the iris and the sclera, UBM has been shown recently to be well suited for in vivo investigations of the zonular apparatus and of accommodation.[40] Further research to determine the impact of swelling of the ciliary body on accommodation after application of the scleral suction ring is needed.

Prolong anesthesia may have influenced our results, especially on day 1. However, there was no significant difference between preoperative and postoperative data at every time point in all measured parameters in the control group, which may rule out the effects of anesthesia. Another point to be clarified is the anatomic differences between rabbit and human eyes. The existence of significant differences of the ciliary body between human and rabbit eyes has been demonstrated with three-dimensional images from very-high-frequency (50 MHz) ultrasound.[33] Compared with human eyes, the rabbit sclera is significantly thinner. The rabbit ciliary body has a small muscular component and very prominent processes. The rabbit ciliary processes are separated by deep valleys with almost vertical sides. Anteriorly, the ciliary processes end abruptly, and approximately every second process leads into an iridial process that runs radially along the posterior surface of the iris. In addition, the rabbit iris is thinner and more delicate than the human iris. The rabbit lens is much larger, and the lens equator attaches directly in one continuous belt at the anterior end of the ciliary processes. In addition, the anterior chamber structures are much shallower in the rabbit than in the human. All these features may accentuate the effect of application of the suction ring in rabbit eyes. Although the anatomy of the rabbit eye differs in many respects from that of the primate eye, rabbit eyes have long been an animal model in the study of glaucoma filtering surgery, retinal surgery, and LASIK.[41–44]

For further confirmation of the findings in this study, the rhesus monkey might provide a more suitable animal model. Although not in human or other primate eyes, this study showed that at least in rabbit eyes, swelling of the ciliary body and shallowing of the chamber angle may be present transiently after scleral suctioning in lamellar refractive surgery. Although all the changes detected by UBM persisted transiently, the possibility of complications due to prolonged suctioning during lamellar refractive surgery are still worthy of concern. Our data suggest that shortening the duration of suctioning during surgery may prevent the development of adverse effects on cilioangular structures. However, caution should be used in direct extrapolation of this rabbit model to the human LASIK procedure. Further long-term and in vivo human studies are needed to confirm the study results.

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EVIDENCE - 5

Effect of Microkeratome Suction during LASIK on Ocular Structures

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Purpose: To study the effect of microkeratome suction on ocular structures during LASIK.

Design: Observational, prospective case series.

Participants: Twenty-one eyes of 11 patients with myopia or astigmatic myopia (8 females, 3 males) were included. The mean patient age was 36.3 years (median, 37 years; range, 24–48 years), and the mean spherical equivalent was −5.03 diopters (D) (median, −4.63 D; range, −2.38 to −8.38 D).

Methods: We performed preoperative and intraoperative A-scan ultrasonography during application of suction using the Hansatome microkeratome (Bausch & Lomb Surgical, Munich, Germany) to create corneal flaps during LASIK. We also performed preoperative and postoperative B-scan ultrasonography of the posterior ocular segment with special attention to the presence and size of posterior vitreous detachment (PVD).

Main Outcome Measures: We measured changes in the axial length, anterior chamber depth, lens thickness, and vitreous distance (distance from the posterior lens capsule to the posterior pole) during application of the microkeratome suction ring and recorded new occurrences of or increases in the size of the PVD after surgery.

Results: The lens thickness decreased (mean change, −0.20 mm; $P = 0.001$; 95% confidence interval [CI], −0.11 to −0.30) in 18 eyes during application of the suction ring. The vitreous distance increased (mean change, 0.20 mm; $P = 0.004$; 95% CI, 0.08–0.32) in 16 eyes. No statistically significant changes were found in the anterior chamber depth ($P = 0.75$) or axial length ($P = 0.51$). After surgery, 3 of 14 eyes (21.4%) experienced PVD that did not have echographic signs of PVD before surgery. Of 7 eyes with preoperative PVD, the PVD enlarged in 1 eye (14.3%).

Conclusions: During application of microkeratome suction, the lens thickness decreases, whereas the vitreous distance increases, suggesting anterior traction on the posterior segment. The relationship between the observed PVD and LASIK merits further investigation. *Ophthalmology 2005;112:645–649 © 2005 by the American Academy of Ophthalmology.*

LASIK currently is the most commonly performed procedure to treat refractive errors. The range of available correction, the reliability and safety of the results, and the speed of visual recovery after surgery made the procedure a revolutionary breakthrough in ophthalmology in the 1990s.

Technical advances have made the microkeratome cut a safe procedure.[1] A suction ring that is applied around the cornea increases the intraocular pressure (IOP) to more than 60 mmHg, creating a firm cornea and permitting a precise corneal flap to be cut, which is followed by laser ablation.[2,3]

Most reported LASIK complications have been related to the refractive outcome or to corneal and anterior segment injury and wound healing; however, posterior segment complications also occur, although they are less common.[4] Some reports have described an association between LASIK and vitreoretinal pathologic features, such as posterior vitreous detachment (PVD), retinal breaks, retinal detachments, macular holes, lacquer cracks, macular hemorrhages, optic neuropathy, and retinal vein occlusion.[4] Some authors theorize that these adverse effects occur as the result of excimer laser shock waves during corneal ablation, whereas others hypothesize that the suction exerted during the keratome cut causes anteroposterior traction that results in pathologic alterations.[5] However, the effects of LASIK on the posterior segment have not yet been determined precisely.

In this study, we examined the effect of microkeratome suction on the ocular globe, because this is the part of the LASIK procedure that is suspected to have the most relevant impact on the posterior segment structures. We theorized that anteroposterior changes in the ocular globe length, alterations of the anterior segment structures (lens thick-

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Prof Kohnen is a consultant to Bausch & Lomb, Inc. Neither author has a financial or proprietary interest in any instrumentation or devices used in this study.

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ness, anterior chamber depth), or both may occur during microkeratome suction.

Patients and Methods

Study Population, Preoperative Evaluation, and Instrumentation

This prospective, observational case series included 21 eyes of 11 patients (8 females, 3 males) with myopia or astigmatic myopia. The mean patient age was 36.3 years (median, 37 years; range, 24–48 years). The study was performed at the Department of Ophthalmology, Johann Wolfgang Goethe-University, Frankfurt, Germany. Inclusion criteria were suitability for LASIK correction of myopia and absence of ocular pathologic conditions and of relevant systemic diseases.

All participants were evaluated for refractive surgical correction after a thorough ophthalmologic examination, including indirect ophthalmoscopy of the posterior segment and laser interferometry (IOL-Master; Zeiss, Jena, Germany) and were found to be suitable candidates for the LASIK procedure. All subjects were informed about the investigative nature of the ultrasound measurements and they provided informed consent. Because of the noninvasive, observational nature of the study, ethics committee approval was not required.

All patients underwent surgery performed by 1 experienced LASIK surgeon (TK) using the Hansatome microkeratome (Bausch & Lomb Surgical, Munich, Germany) to create a superiorly hinged corneal flap using a 20.3-mm suction ring and 9.5-mm intended flap diameter. The excimer laser ablation was performed with a Technolas C-LASIK 217Z-Laser (Bausch & Lomb Surgical).

A-Scan Ultrasound Biometry

After conventional preoperative preparation and positioning and immediately before applying the microkeratome ring, 3 A-scan ultrasound biometry measurements of the axial length, anterior chamber depth, lens thickness, and vitreous distance (defined as the distance between the posterior lens capsule and the posterior pole) were performed by the surgeon. The microkeratome then was positioned, the suction was initiated, and balanced saline solution drops were administered. After confirming the appropriate position of the microkeratome and ensuring an IOP of more than 60 mmHg using applanation tonometry, the ultrasound A-scan measurements were repeated quickly 3 times. The flap was created, followed by excimer laser ablation and flap repositioning. Of the 3 measurements at each time point, 1 was selected according to the ultrasound pattern and the agreement of the axial length with laser interferometry measurements. Laser interferometry matching was performed in presuction measurements only.

B-Scan Ultrasonography

Immediately before entering the operating room, ocular sonography (B-scan; I^3 System ABD; I^3 Innovative Imaging Inc., Sacramento, CA) was performed by an experienced ocular sonographer with specific attention to the vitreous body and to the prevalence, location, and size of the PVD. The procedure was carried out with patients in the supine position using a standard eyelid contact method without topical anesthesia and with high to maximal gain to detect and localize the ultrasonographic PVD signs, namely, a low-reflection mobile membrane or ring at the vitreous base and partial or complete detachment from the posterior pole. All images were saved electronically for postinterventional comparison. This procedure was repeated in all patients 1 week after surgery to detect vitreoretinal alterations. Because an exact assessment of the changes in the size of the PVD was not possible, the sonographer was asked to consider that progression occurred only when detachment of a new quadrant or involvement of the posterior pole was apparent. Regular postoperative ophthalmologic examinations were performed on days 1 and 7 and 1 month after surgery.

Data Collection and Statistical Analysis

All data were collected and evaluated by the same person (AM) using Microsoft Excel (version 9.0)[6] and SPSS for Windows (version 10.0) programs.[7] P values less than 0.05 were considered statistically significant.

For the A-scan measurements, the mathematical differences between the intraoperative and preoperative values were calculated for the anterior chamber depth, lens thickness, axial length, and vitreous distance. Besides the descriptive statistics, the Wilcoxon matched pairs test was performed to detect statistical significance.

In the B-scan studies, the number and percentage of new PVDs and increases in preoperatively observed PVDs were assessed. In a subgroup without preoperative echographic PVD signs, the incidence of PVD was compared with that in a subsequent age- and refraction-matched group that did not undergo intraoperative A-scan measurement and therefore had a shorter suction time.

Results

The mean spherical equivalent was −5.03 diopters (D; median, −4.63 D; range, −2.38 to −8.38 D), and the mean axial length (IOL-Master) was 25.08 mm (median, 25.06 mm; range, 24.18–26.79 mm). Table 1 shows the patient data.

A-Scan Ultrasound Biometry

The lens thickness decreased during application of microkeratome suction in 18 eyes (85.7%; mean decrease, −0.20±0.21 mm; P = 0.001; median decrease, −0.2 mm; range, +0.27 to −0.72 mm; 95% confidence interval [CI], −0.11 to −0.3 mm). The vitreous distance increased in 16 eyes (76.2%; mean increase, 0.20±0.26 mm; P = 0.004; median increase, −0.19 mm; range, +0.77 to −0.2 mm; 95% CI, 0.08–0.32 mm). There were no statistically significant changes in the axial length (mean change, −0.01 mm; P = 0.51) or the anterior chamber depth (mean change, −0.01 mm; P = 0.75; Table 1). A post hoc power calculation of nonsignificant parameters (axial length and anterior chamber depth) revealed a power of 0.0943 and 0.0499, respectively. Proposing a desired power of 0.90, the required sample size for statistical proof of the observed difference is calculated at n = 505 for the axial length and n = 2136 for the anterior chamber depth. Therefore, the study was not adequately powered to detect a difference in their measures if there was a difference of 0.01 mm.

B-Scan Ultrasonography

Before surgery, 14 of 21 eyes (66.7%) had no echographic signs of PVD. The remaining 7 eyes (33.3%) had partial PVD, detected by ultrasound, of which 1 eye had an enlarged PVD (14.3%). The PVD in the temporal and inferior quadrants before surgery extended toward the central region, including the posterior pole. After surgery, 3 of 14 eyes without preoperative echographic signs of a PVD experienced a partial PVD (2 patients; 21.4%; 95% CI, 4.7–50.8; Table 1). In an age- and refraction-matched group that

Table 1. Difference between Intraoperative and Preoperative A-Scan Ultrasound Measurements and B-Scan Examinations*

Patient No.	Age (yrs)	Gender	Eye	Spherical Equivalent (D)	Axial Length/ Laser Interferometry	Axial Length Difference (mm)	Anterior Chamber Depth Difference (mm)	Lens Thickness Difference (mm)	Vitreous Distance† Difference (mm)	Preoperative B Scan Results	Postoperative B Scan Results
1	48	M	L	−2.38	24.47	0.02	0.19	−0.36	0.19	No PVD	No change
2	36	F	R	−3.00	24.56	−0.16	−0.19	−0.21	0.24	No PVD	No change
3	38	F	R	−3.25	24.48	−0.10	0.15	−0.15	−0.1	PVD nasal	No change
4	38	M	R	−3.38	25.06	0.46	0.00	−0.31	0.77	No PVD	No change
5	36	F	L	−3.50	24.79	−0.07	−0.05	−0.11	0.09	No PVD	No change
6	38	F	L	−3.63	24.47	0.29	0.72	−0.72	0.29	PVD nasal	No change
7	48	M	R	−3.75	25.30	0.22	0.10	−0.46	0.58	No PVD	No change
8	36	F	L	−4.38	24.18	0.09	−0.19	−0.05	0.33	No PVD	No change
9	42	F	L	−4.50	25.11	−0.21	0.10	−0.31	0.0	PVD	No change
10	42	F	R	−4.50	25.16	0.08	0.38	−0.10	−0.2	PVD	No change
11	28	F	L	−4.63	24.78	−0.11	0.19	−0.20	−0.1	No PVD	PVD inf.
12	28	F	R	−4.63	24.97	−0.08	0.19	−0.31	0.04	No PVD	PVD inferior/ nasal inferior
13	38	M	L	−4.75	25.64	−0.26	−0.05	−0.26	0.05	No PVD	No change
14	36	F	R	−5.25	24.48	−0.00	0.09	0.05	−0.14	PVD temporal/ superior	No change
15	39	F	L	−5.50	25.20	−0.16	−0.05	−0.25	0.14	No PVD	No change
16	39	F	R	−5.88	25.58	−0.05	−0.19	−0.10	0.24	No PVD	PVD superior
17	24	F	R	−7.13	24.82	0.14	−0.24	−0.15	0.53	No PVD	No change
18	24	F	L	−7.63	25.15	0.11	−0.77	0.26	0.62	No PVD	No change
19	34	M	R	−7.63	25.86	−0.15	−0.39	−0.05	0.29	PVD temporal	No change
20	34	M	L	−8.00	25.89	−0.11	−0.20	0.00	0.09	No PVD	No change
21	37	F	L	−8.38	26.79	−0.17	−0.05	−0.46	0.34	PVD temporal/ inferior	PVD temporal/ inferior/central

F = female; L = left; M = male; PVD = posterior vitreous detachment; R = right.
*Data sorted by spherical equivalent.
†Distance from the posterior lens capsule to the posterior pole.

had no preoperative echographic PVD signs and that did not undergo intraoperative A-scan measurement (shorter suction time), we observed 1 case of new PVD. However, the difference between both groups was not statistically significant.

Discussion

The high number of refractive surgical procedures performed, with LASIK being the most popular, has led to an increasing awareness of its side effects and potential complications. Posterior segment complications resulting from LASIK have been reported in rare cases.[4] Large studies have shown no greater incidence of retinal detachment after LASIK compared with the reported incidence of retinal detachment in patients with myopia who have not undergone refractive surgery.[4,8,9] However, a number of reports have been published on posterior segment complications directly associated with LASIK.[4] Several pathogenetic theories have been postulated, of which the potential changes in the shape of the ocular globe caused by application of the microkeratome seems to be the most contributory.[5] The application of the suction ring and the rapid increase in IOP, which is necessary to stabilize the anterior segment just before flap creation, may lead to a change in the shape of the anterior segment, displacement of the lens, compression and decompression of the posterior segment structures by conduction of power via the vitreous body or sclera, or all of these. Possible results are anteroposterior traction or compression potentially leading to posterior segment complications—for example, retinal tears. None of these theories has been assessed in a study, and the effects of LASIK on the posterior segment are not known with certainty.

In the present study, we quantified the effect of microkeratome suction on the ocular globe structures in vivo. The consistent decrease in lens thickness and increase of vitreous distance (posterior lens capsule to retina) that we observed underscore the power of the microkeratome to affect the ocular architecture. The decrease in lens thickness is comparable with displacement of the lens in the anterior direction along with the anterior hyaloid. This may accelerate vitreous detachment and cause traction at the vitreous base, the posterior pole, or both, where the junction between the vitreous body and the retina is tight. This phenomenon may explain the retinal breaks, retinal detachments, macular hemorrhages, and lacquer cracks reported by others and the PVDs that we observed.

Luna et al[10] reported the development of PVD after LASIK with an incidence of 2% in a group of 50 patients with low myopia (−1.25 to −3.5 D) and 24% in a group of 50 patients with high myopia (−6 to −10 D). Considering the data from the 100 eyes, this corresponds to 13%; thus, there is not a great deal of difference between our results and the data in the literature. No definitive answer was found, however, regarding the incidence and risk factors associated with this phenomenon, because the number of

eyes in the present study was too small to determine exact incidence rates (see 95% CIs). Furthermore, we should consider that closed lids may lessen the sensitivity of B-scan sonography in detecting PVD; thus, some changes might not have been detected. Performing intraoperative A-scan measurements requires longer suction periods than in routine LASIK procedures, which may result in an increased risk of PVD. A comparison with an age- and refraction-matched group without intraoperative A-scan measurement did not reveal a statistically significant difference. However, this is, most probably, the result of the small sample size in our study. Thus, our B-scan results need to be verified by future studies with a larger number of cases. Nevertheless, we recommend adding the development of PVD to the informed consent form and to advise patients, particularly those with higher myopia, about the nature, symptoms, and consequences of PVD.

Mostafavi et al,[11] who reported the preliminary results of A-scan measurement from 6 cadaver porcine eyes during application of microkeratome suction, observed a mean shortening of the ocular globe of 0.67 mm. In contrast, Flaxel et al[12] observed an increase in axial length and no change in the anterior chamber depth after application of the suction ring in 8 human eyes from an eye bank. Neither finding was confirmed in our study in vivo, because no statistically significant change in the axial length was found. The axial length measurements in cadaver eyes outside the orbital cavity, as performed by both above-mentioned study groups, may differ from those performed in vivo and therefore may provide less relevant data. However, our results corroborate the hypothesis of Flaxel et al regarding the presence of anterior traction caused by displacement of the vitreous body during suction but not caused by ocular globe elongation.

Our study did not reveal a statistically significant alteration in the anterior chamber depth. This finding is important, as is the observation that the axial length was insignificantly altered. Any systematic mistake, such as tilting of the ultrasound probe during intraoperative measurements, would result in systematically different axial length and anterior chamber depth measurements. The increase in the vitreous distance is a result of a decrease in the lens thickness, when considering that the axial length and the anterior chamber depth remained unchanged.

Based on the available data, the mechanics of microkeratome-induced alterations in ocular structures can be described as follows. Application of the suction ring beneath the limbus leads to circular traction on the sclera, the adjacent ciliary body, and the zonula ciliaris, resulting in traction on the equatorial region of the lens, which by itself causes a decrease in lens thickness (the opposite effect of accommodation). In young patients, usually less than 40 years of age, the posterior capsule of the lens strongly adheres to the anterior hyaloid. The decrease in lens thickness, similar to the displacement of the lens anteriorly, is accompanied by a forward movement of the anterior hyaloid, causing traction at the vitreous base, the posterior pole, or both. This theory also explains how vitreoretinal traction is generated by a change in the lens architecture without substantial lengthening of the eye. In fact, many of the reported posterior segment complications of LASIK may be related to the traction on the vitreous body and the consequent conduction of the power vector to the retina. The development of PVD, as seen in our study, supports the hypothesis that there must have been some traction applied to the posterior segment.

The mean changes in lens thickness and vitreous distance (0.2 mm) appear too small to cause vitreoretinal alterations. However, the range of up to −0.72 mm for the lens and +0.77 mm for the vitreous body highlights the relatively high interindividual deviations. Furthermore, this effect may be much higher when suction is initiated and released after the flap is created. In fact, the rarity of vitreoretinal complications associated with LASIK[4,8] makes clear that the power that causes them must be low and harmless for normal vitreoretinal consistency. Certain predisposing factors are necessary for the occurrence of complications that are caused by a mild amplitude of traction.

In this study, the A-scan measurements were performed with direct contact between the probe and the cornea without a water funnel (no immersion technique). The direct contact with the corneal surface has the potential danger of depressing the cornea, thereby resulting in smaller inaccurate measurements of the anterior chamber depths and axial lengths. This is of special interest when considering that during microkeratome-induced suction, the cornea becomes firmer and deformation of the anterior chamber by the probe is less likely than during the preoperative normal tension A-scan assessment.

An important step in flap creation is cutting through the cornea. This occurs during the suction period. During this phase, the cornea and the anterior chamber are subject to pressure from the microkeratome. As a consequence, the IOP rises even more and the ocular structures may be affected during flap creation in ways not experienced during the suction period before flap creation. We did not study the alterations caused by this specific part of the microkeratome application. The effect of excimer laser waves on the posterior segment seems to be low, as shown by Krueger et al.[13] Although the vitreoretinal complications of LASIK are most likely related to the mechanics of microkeratome application, a contributory effect of the excimer laser shockwave cannot be ruled out.

The mechanics of microkeratome suction can be compared to that of blunt ocular trauma when the ocular globe is compressed and quickly released.[14,15] The range of LASIK-related posterior segment complications is similar to that of blunt ocular trauma, however, at a much lower level incidence and degree.

Major limiting factors of our study were the static nature of A-scan ultrasound biometry, which delivers information at a very specific moment, namely, as the suction is applied, and the limited number of eyes for the determination of the exact incidence and risk factors for the occurrence of PVD (B-scan assessment). A dynamic online evaluation of the axial length and lens thickness would deliver interesting data at the time of suction initiation and release. Furthermore, we included only myopic eyes in this study, and the ocular changes in hyperopic eyes may be different.

Further examination of microkeratome mechanics and the effect on the ocular structures is necessary to understand

thoroughly the impact of LASIK on the posterior segment of the eye.

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EVIDENCE - 6

Proposed Mechanism for Retinal Tears after LASIK

An Experimental Model

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Objective: To demonstrate axial length changes associated with anterior shift of the lens/iris diaphragm and anterior vitreous base in human cadaver eyes during suction ring application preceding Moria LASIK, and to propose that these changes may be associated with anterior retinal tears.

Design: Human eye study.

Materials: Eight human eye bank eyes ranging in age from 65 to 73 years. Two eyes had a history of intraocular surgery involving cataract extraction and intraocular lens implantation.

Intervention: Measurements of intraocular pressure via internal manometer and Tono-Pen, anterior chamber depth, and axial length before and after application of a Moria LASIK suction ring.

Main Outcome Measures: Change in anterior chamber depth and axial length after Moria LASIK suction ring application.

Results: Axial length increases (mean change = 1.125 mm, $P = 0.02$) after application of the suction ring, whereas anterior chamber depth shows no significant difference (mean change = −0.01 mm, $P = 0.98$), suggesting anterior movement of the vitreous base resulting in traction on the anterior retina.

Conclusion: Axial length increase with anterior displacement of the vitreous base during suction ring placement might predispose susceptible eyes to anterior retinal tears during and after LASIK. *Ophthalmology 2004;111:24–27 © 2004 by the American Academy of Ophthalmology.*

Laser in situ keratomileusis for the correction of various levels of myopia has become increasingly popular over the past 6 years. It is becoming more useful for the correction of moderate to high myopia, and is being used with increasing frequency to correct even highly myopic eyes. The anterior segment complications have been well documented and reported in the literature.[1,2] As the use of LASIK has become more common, there have been several reports proposing a relationship between LASIK and retinal detachments in these myopic eyes.[3–6]

We developed a model utilizing human eye bank eyes to demonstrate changes in the axial length of the eye during application of the Moria (Paris, France) LASIK suction ring, and propose a mechanism for the development of retinal tears in susceptible myopic eyes.

Patients and Methods

In this experimental model using human eye bank eyes, we prospectively evaluated changes in several parameters before, during, and after the application of a Moria LASIK suction ring.

Before placement of the suction ring, intraocular pressure (IOP) was measured using a manometer manufactured by Precision Dynamics (San Fernando, CA) (Fig 1). This device was left in place for the duration of the measurements. Intraocular pressure was also measured before and after suction ring placement via a Tono-Pen XL handheld tonometer (Mentor, Norwell, MA). Anterior chamber depth and axial length measurements were monitored before and after suction ring placement with a Humphrey Ultrasonic Biometer manufactured by Humphrey Instruments Inc. (San Leandro, CA).

Measurements were recorded from 8 consecutive human eye bank eyes ranging in age from 65 to 73 years obtained from the Loma Linda University Medical Center Eye Bank (Table 1). Two eyes had a history of intraocular surgery, consisting of cataract

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The authors have no proprietary interest in any of the instruments or procedures used in this project.

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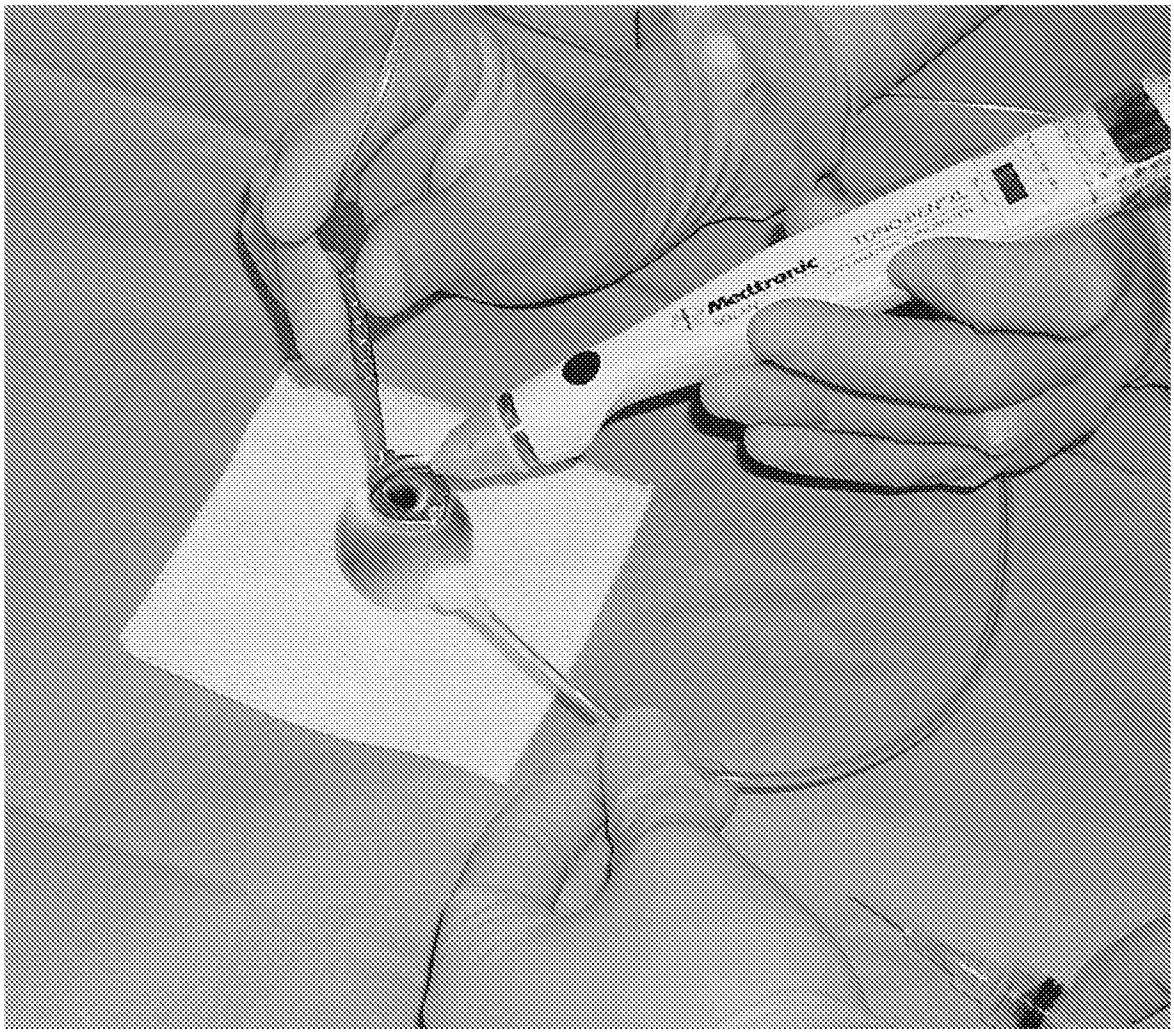

Figure 1. Tono-Pen intraocular pressure measurements with suction ring and intraocular manometer in place. This image was manipulated with 3-dimensional animation to help demonstrate the procedure.

extraction with intraocular lens implantation at least 1 year before enucleation. No eyes had a history of ocular trauma. The number of days after removal ranged from 2 to 14 days, and all eyes were kept in moist chambers, unpreserved, until the experiments were carried out on a single day.

Results

Results are summarized in Table 1. Axial length measurements increased (mean change = 1.125 mm, $P = 0.02$) after application of the suction ring, whereas anterior chamber depth showed no significant difference (mean change = −0.01 mm, $P = 0.98$) before and after suction ring placement (Fig 2). The Humphrey Ultrasonic Biometer was not able to monitor the anterior chamber depth for human eye bank eyes 03-0515 and 03-052, both having the status post–cataract surgery, though it was accurately able to monitor the axial length measurements. The postsuction anterior chamber depth reading on eye 04-028 was not available, due to a technical difficulty. These values were not included in the final statistical analysis (Table 1).

Intraocular pressure increases ranged from 30 to 50 mmHg after suction ring placement (mean change = 40.9 mmHg, $P<0.0001$). These IOP rises have been previously documented.[7,8] There was a difference noted between the direct measurements as made by the intraocular method (manometer) and the external method (Tono-Pen) after application of the suction ring, with higher measurements demonstrated by the Tono-Pen method.

Discussion

Refractive surgery for the correction of ametropia, especially myopia, is well established, but these procedures may

Table 1. Changes in Intraocular Pressure (IOP), Axial Length, and Anterior Chamber (AC) Depth before and after Moria LASIK Suction

Eye ID #	Change in IOP (mmHg)	Baseline Axial Length (mm)	Postsuction Axial Length (mm)	Baseline AC Depth (mm)	Postsuction AC Depth (mm)
04-0130	30	23.34	25.83	2.73	2.20
04-0140	42	21.97	23.31	4.60	3.80
04-0270	45	22.00	21.80	2.46	3.73
04-0280	38	22.64	21.83	4.53	NA
03-0515	50	22.73	24.26	NA	NA
03-0520	40	22.53	24.13	NA	NA
04-0152	42	22.29	24.15	2.86	2.60
04-0162	40	22.79	23.98	2.06	2.33

NA = not available.
Mean change in IOP = 40.9 mmHg (standard deviation [SD] = 5.7), $P<0.0001$.
Mean change in axial length = 1.125 mm (SD = 1.092), $P = 0.02$.
Mean change in AC depth = −0.01 mm (SD = 0.82), $P = 0.98$.
Statistical tests were calculated using the paired t test; $P<0.05$ is statistically significant.

lead to complications. Ongoing discussion in the literature since the advent of refractive surgery has shown concern with the possibility of retinal tears and detachments after refractive surgical procedures, though these cases may represent the normal increased incidence of retinal complications in the myopic eye.[6,9–12] Laser in situ keratomileusis has been the refractive procedure of choice for the correction of moderate to high degrees of myopia. Many clinical studies have demonstrated the efficacy and predictability of this procedure with a low complication rate, with most of the complications related directly to the procedure itself and involving primarily the anterior segment of the eye.[1,2,13,14]

There have been recent reports of associations between LASIK and posterior segment pathology, leading to an increased interest in the potential causal relationship between LASIK and posterior segment pathology.[6,15–20] We undertook an experimental study in an attempt to demonstrate physical changes occurring within the eye that could explain the development of post-LASIK retinal pathology.

The exact mechanism used for performing LASIK involves an excimer laser and a microkeratome that has a pneumatic suction ring. The suction ring is a circular chamber that fixates the eye by means of a vacuum. The underside of the fixation ring has a vacuum chamber that seals against the globe. According to the manufacturer, the IOP must exceed 65 mmHg to obtain a resection that is uniform, regular, and of the appropriate diameter. Ozdamar and colleagues have proposed and shown that the shock wave generated by the impact of the excimer energy on the cornea can generate a pressure of up to 100 atmospheres, resulting in mechanical stress on the eye.[5,21] Several studies have looked at the basic science of the pressure waves within the eye.[22,23] These authors propose a potential for shock waves generated in the anterior segment to affect structures in the posterior segment, as has also been proposed by Charteris and colleagues.[3–6,22,23]

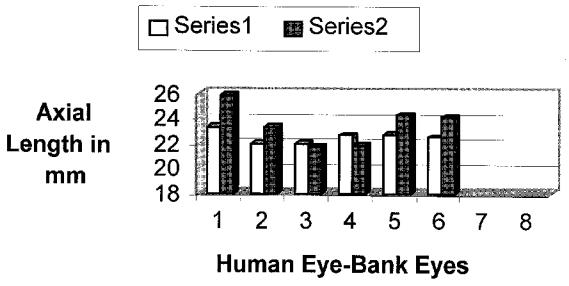

Figure 2. Changes in axial length before (series 1) and after (series 2) Moria LASIK suction ring.

Other factors besides the degree of myopia may also play a role in the incidence of posterior segment pathology. Some are the difference in the design of each microkeratome as well as different rates of vacuum rise and different maximum vacuum levels between microkeratomes. Other variables, such as photoablation spot size and rate of pressure release by the microkeratome, may also be important.

In the present study, we demonstrate the actual increase in axial length measurements after the placement of the suction ring without change in the anterior chamber depth, utilizing an A-scan ultrasound unit. This would indicate that the elongation of the eye is primarily due to a change in the dimensions of the vitreous cavity, rather than a change in the depth of the anterior chamber. A similar mechanism has recently been proposed by Arevalo and colleagues in an editorial in *Ophthalmology*.[6] These changes in the dimensions of the eye could induce a posterior vitreous detachment (PVD) as well as place traction on areas of lattice degeneration located in the anterior retina. Careful follow-up in these cases is warranted, as retinal tears and detachments can occur up to 6 months or even longer after the initial event.[24–27]

Further studies are underway comparing preoperative and postoperative incidences of PVDs in eyes undergoing LASIK. El-Agha and coauthors reported their preliminary unpublished data at the 2001 Vitreous Society meeting; they found a 10% incidence of PVD in moderate myopes (2.25 to –5.75 diopters [D]) and an even greater incidence of PVD in high myopes (−7.50 to −11.00 D) after LASIK.

We have proposed a mechanism by which LASIK may precipitate the development of a retinal tear or detachment in susceptible myopic eyes. We feel that although retinal detachment after LASIK may be uncommon and no cause–effect relationship between LASIK and retinal detachment has been proven, the possibility exists, based on the findings of the present study that LASIK has the potential to aggravate pre-existing retinal pathology and precipitate an acute PVD or retinal tear in areas of pre-existing retinal pathology. It may be beneficial for at-risk eyes of highly myopic patients scheduled for LASIK to have a careful dilated retinal examination with scleral depression to identify high-risk lesions, especially if these patients relate any symptoms of vitreous syneresis. These patients should receive preoperative counseling regarding the risk of retinal problems with or without the LASIK procedure. It is not clear at this time which eyes, if any, would benefit from prophylactic

treatment for retinal pathology, and further research is needed into this topic. Definitely, patients with eyes with subclinical retinal detachments should be discouraged from proceeding with LASIK, whereas patients with eyes with only lattice degeneration and no retinal holes, or only atrophic holes, may need only counseling and no pre-LASIK treatment. These patients should be made aware that LASIK corrects only the refractive component of myopia, and that myopic eyes have the anatomical potential for serious complications with or without undergoing the LASIK procedure.

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EVIDENCE - 7

CLINICAL AND EXPERIMENTAL
OPTOMETRY

ORIGINAL PAPER

Dry eye after LASIK: Comparison of outcomes for Asian and Caucasian eyes

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Background: Dry eye is a common complication of LASIK surgery. Our clinical impression was that post-LASIK dry eye was more problematic for our Asian patients. The aim of this study was to determine if dry eye after LASIK is more prevalent, more sustained and more severe in Asian eyes compared with Caucasian eyes.

Methods: This study was based on a retrospective analysis of a clinical database. Data (n = 932 eyes, 932 patients) was collected before and after (week 2 and months 1, 3 and 6) LASIK surgery. Patients were defined as Asian if both parents were of East Asian ethic origin. Assessments included dry eye symptoms, ocular surface staining, tear volume, tear secretion, tear film stability and corneal sensation.

Results: Asian eyes had greater ocular surface staining, poorer tear film stability and lower tear volume before LASIK and at all times after LASIK. Dry eye symptoms occurring 'often or constantly' were more prevalent at all time points after LASIK in Asian eyes. Chronic dry eye persisting six months or more after LASIK was diagnosed in 28 per cent of Asian eyes and 5 per cent of Caucasian eyes ($p < 0.001$). Asian patients with chronic dry eye were predominantly female, reported dry eye symptoms, had greater ocular surface staining and lower tear secretion, stability and volume before surgery. After LASIK, Asian eyes had a slower return to pre-operative values for ocular surface staining, tear volume and corneal sensation.

Discussion: The risk of chronic dry eye after LASIK was significantly higher in Asian eyes. Contributing factors could include racial differences in eyelid and orbital anatomy, tear film parameters and blinking dynamics and higher attempted refractive corrections in Asian eyes.

Key words: Asian eye, dry eye, LASIK, myopia

Dry eye preventing safe and comfortable contact lens wear is a major motivating factor for patients considering refractive surgery.[1] Dry eye is considered by refractive surgeons to be the most common complication of LASIK surgery.[2] Cutting a LASIK flap and performing a stromal ablation disrupts the corneal innervation and produces a relative loss of corneal sensation for up to six months after surgery.[3-6] This loss of corneal sensation appears to be a significant contributing factor to the reduction in tear secretion, tear film stability, tear clearance, blink rate, conjunctival goblet cell density and the increase in tear osmolarity and punctate epitheliopathy of the post LASIK eye.[4,6-11] In patients with dry eye before LASIK,[11] in long-term contact lenses wearers[4,9] and in those having deeper surgical ablations[5] and superior hinged flaps,[6] the return of corneal sensation to levels observed before surgery appears to take longer than six months and is associated with more persistent dry eye signs and symptoms.[4,6,9]

Recent studies[12-14] have suggested that dry eye is more prevalent in Asian

populations than in Caucasians. Clinically, we had formed the impression that sustained dry eye after LASIK was more common in our Asian patients. This observation was of concern to us as the prevalence of myopia is much higher in Asians than in Caucasians[15,16] and appears to be increasing in urbanised Asian communities.[17] LASIK continues to be the dominant refractive surgery procedure for myopia,[18] therefore it is likely that increasing numbers of myopic Asians will seek refractive surgery. In this study, we analysed our clinical patient database to compare Asian and Caucasian patients after LASIK. The aims of the analysis were to determine if dry eye after LASIK is more prevalent, more severe and more sustained in Asian eyes.

METHODS

The study was a retrospective analysis of 932 patients who underwent LASIK for correction of myopia and myopic astigmatism at Excimer Laser Vision Centre, Brisbane, Australia, between August 1998 and December 2002. Our database tracks surgical outcomes for all myopic LASIK procedures and contained a total of 1,886 LASIK procedures, of which 1,846 were primary LASIK procedures on 1,026 patients. Of these, 932 patients met the inclusion criteria and had complete data for at least one eye for 12 months. Data analysis was based on these 932 patients. In patients who had surgery on both eyes, only the right eye data were analysed, provided the data were complete and the inclusion criteria were met. All patients received a detailed explanation of the procedures involved in the study and provided written informed consent. The Queensland University of Technology Human Research Ethics Committee provided written approval of the study protocol.

The eligibility criteria used in the study were:

- no autoimmune disease, metabolic disease or uncontrolled systemic disease
- no active disease of the external eye or adnexae
- no intraocular disease
- no degenerative or neurotrophic corneal disease
- no pre-operative or post-operative use of topical medications other than those prescribed
- no previous ocular surgery or trauma
- not pregnant or breastfeeding
- stable refraction for at least 12 months prior to LASIK
- stable keratometry and pachymetry following cessation of contact lens wear
- no lenticular opacities identified before or after surgery that were deemed to have a significant effect on the refractive outcome
- compliance with prescribed tear film and ocular surface management before and after surgery.

Patients were defined as Asian if one or both parents were of East Asian ethic origin (for example, Chinese, Japanese, Thai, Filippino, Vietnamese, Korean, Taiwanese, Singaporean, Malaysian). To avoid complicating the analysis, we excluded patients who had partial Asian ancestry. We also excluded patients of Indian Asian ancestry.

Pretreatment of the tear film and ocular surface was performed on indication where specific tear film and ocular surface problems were identified before LASIK. Pre-treatment measures included:

1. Non-preserved artificial tears, gels or ointments; non-preserved steroid (prednisolone sodium phosphate 0.5 per cent or 1 per cent hydrocortisone ointment) for ocular surface inflammation and/or eyelid margin inflammation.
2. Silicone punctal plugs (Flexplug, Eagle Vision, Memphis USA) for tear deficiency, where artificial lubricants alone were insufficient.
3. Lid hygiene procedures for eyelid disease.

All LASIK procedures were performed by one experienced LASIK surgeon (LL) using a surgeon-adjusted ablation nomogram. The lamellar flaps were created using the automatic corneal shaper (Chiron Vision, Irvine, USA) and the excimer laser (Nidek EC-5000, Nidek, Gamagori, Japan) performed the stromal ablations. The flaps were 8.5 mm wide and 130 µm thick with an optic zone of 5.5 to 6.5 mm and a transition zone of 7.5 mm. After surgery, all eyes received a standard treatment of non-preserved chloramphenicol 0.5 per cent (Chauvin Pharmaceuticals, Essex, UK) four times per day for three days and fluorometholone acetate 0.1 per cent (Flucon, Alcon Laboratories, Fort Worth USA) four times per day, tapering one drop per week over one month. All patients were instructed to use non-preserved artificial tears (Cellufresh [sodium carboxymethylcellulose 0.5 per cent in lactate buffer, non-preserved, Allergan, Irvine USA] and/or Bion Tears [hydroxypropyl methylcellulose 0.3 per cent, Dextran 70 0.1 per cent in bicarbonate buffer, Alcon Laboratories, Fort Worth USA]) at least every two hours for the first month after surgery and then at least four times per day for the 12 months after surgery.

Patients were also instructed to use sodium carboxymethylcellulose 1.0 per cent in lactate buffer, non-preserved (Celluvisc, Allergan, Irvine USA) for at least one week after LASIK as a night-time lubricant and, if long-term night-time lubrication was required, then Celluvisc or carbomer gel, non-preserved (Polygel, Alcon Laboratories, Fort Worth USA) or paraffin plus lanolin, non-preserved ointment (Polyvisc, Alcon Laboratories, Fort Worth USA) were prescribed. Silicone punctal plugs were inserted in the inferior puncta of tear deficient eyes non-responsive to the lubricant therapy described above.

Assessments

The following assessments were performed on each patient before surgery and at two weeks, and one, three and six months post-LASIK with the results recorded in the clinical database:

1. **Fluorescein break-up time** (FBUT): a measure of tear film stability, was performed using the method described by Cho and Brown.[19]
2. **Schirmer I test** (Colorbar, Eagle Vision, Memphis USA): a measure of reflex tear secretion was performed without anaesthetic using standard methods.[20] The Schirmer test was not performed at week 2 to avoid interference with flap healing.
3. **Phenol red thread tear test** (PRT) (Zone Quick Menicon Co Ltd, Nagoya Japan): a measure of tear secretion, volume and turnover was performed using the methods previously described.[21]

Nationality	Number of subjects (n = 54 total)
Chinese	25
Vietnamese	7
South Korean	6
Indonesian	5
Japanese	4
Taiwanese	2
Singaporean	2
Malaysian	2
Filippino	1

Table 1. Nationality of ancestry in Asian patient group

4. **Ocular surface staining**: fluorescein ocular surface staining was graded by the Oxford grading scheme on a scale of zero to five using methods previously described.[22]

5. **Corneal sensation**: central corneal sensation was measured using the Cochet-Bonnet aesthesiometer (Luneau Ophthalmologie, Charters, France).[23]

6. **Dry eye symptoms**: dry eye symptoms were assessed using the McMonnies Dry Eye Symptom Survey, a validated dry eye symptom survey.[24] Patients were classified as having dry eye symptoms (either before or after surgery) if they reported experiencing one or more of the primary symptoms in the survey (soreness, scratchiness, dryness, grittiness, burning) occurring often or constantly.

7. **Refractive outcome**: defined as the difference between the spherical equivalent refraction and the target spherical equivalent refraction.

Patients were questioned on their history of contact lens wear. Patients were classified as contact lens wearers before surgery, if they wore lenses on a regular basis (minimum average wearing time of 30 hours per week) and had worn contact lenses for at least the past year. Occasional or intermittent contact lens wearers were regarded as non-contact lens wearers for the purpose of this study.

In accordance with standard criteria,[20] patients were diagnosed as having dry eye before or after surgery, if they experienced one or more of the McMonnies dry eye primary symptoms occurring 'often' or 'constantly', their FBUT was less than 10 seconds and they had a fluorescein corneal staining score of one or more. Patients were diagnosed as having chronic dry eye if they had dry eye (according to the definition above) for a period of six months or more after surgery. The six-month cut-off point was chosen because at six months, the majority of studies indicate that dry eye parameters such as dry eye symptoms,[8] tear film stability,[8,10] ocular surface staining,[8,9] tear volume,[8] tear secretion[9,10] and corneal sensation[3-6] have returned to pre-operative levels.

Statistical analysis

Parametric tests were used to analyse refractive data. Other ocular variables were analysed using non-parametric tests because of the non-normal distribution of the data. Comparisons between groups and between variables were made using the Pearson Chi Square Test for categorical data and the ANOVA or the Kruskall-Wallis ANOVA tests for continuous data. Differences were considered significant when $p < 0.05$.

RESULT

Overall patient demographics

For the 932 patients, the mean spherical equivalent refraction was -4.6 ± 2.8 D (sphere -3.78 ± 2.19 D [minimum -1.00; maximum -16.50], cylinder -0.68 ± 0.91 D [minimum 0.00; maximum -6.50]). Mean ablation depth for all patients was 59 ± 27 µm (minimum 15; maximum 161).

Mean patient age was 36 ± 9 years (minimum 18; maximum 65) and 56 per cent (522/932) of patients were female. Before LASIK surgery five per cent (47/932) of the patients were diagnosed with dry eye and a further 16 per cent (151/932) reported dry eye symptoms but did not have significant dry eye signs. Following surgery, seven per cent (65/932) of patients were affected by chronic dry eye.

Comparison of patient characteristics: Asian and Caucasian groups

Asian patients comprised six per cent (54/932) of patients. Chinese patients formed 46 per cent of the Asian group. The breakdown of nationalities of the Asian patients is given in Table 1. Patient characteristics for Asian and Caucasian patients are presented in Table 2. The Asian group had significantly more females, higher attempted refractive corrections and greater total ablation depths compared to the Caucasian group. There were significantly more contact lens wearers in the Asian group. The percentage of subjects diagnosed with dry eye before surgery and the percentage receiving pretreatment was not significantly different between the groups.

Comparison of intra-operative and post-operative complications and refractive outcomes: Asian and Caucasian groups

There were no significant differences between Asian and Caucasian eyes with respect to intra-operative and post-operative complications (Table 3). The difference between the spherical equivalent of refraction and the target refractive outcome was not significantly different between Asian and Caucasian eyes at any time after surgery.

Comparison of chronic dry eye prevalence after LASIK

Asians eyes had a higher prevalence of chronic dry eye after LASIK (28 per cent [15/54] compared with five per cent [41/878] for Caucasian eyes, [$p < 0.001$]). Asian patients with chronic dry eye were predominantly female, reported dry eye symptoms, had greater ocular surface staining and poorer tear secretion, tear film stability and tear volumes before surgery (Table 4).

Comparison of dry eye outcomes in Asian and Caucasian groups matched for surgical ablation depth

To eliminate bias in the results due to the Asian patients having a greater pre-operative myopic correction and therefore greater total ablation depth compared to

the Caucasians, we examined a subgroup of patients where the Asian (n = 48) and Caucasian (n = 407) patients were matched for surgical ablation depth. The subject demographics of this subgroup are given in Table 5. With this adjustment for refractive ablation, the prevalence of chronic dry eye was 25 per cent (12/48) in Asian eyes and seven per cent (29/407) in Caucasian eyes. Comparisons of the prevalence of dry eye symptoms and of tear film and ocular surface parameters before and after surgery for the surgical ablation depth matched Asian and Caucasian groups are given in Table 6.

Before LASIK, there were no significant differences in the percentages of patients in the Asian and Caucasian groups reporting dry eye symptoms often or constantly. Dry eye symptoms were significantly more prevalent in Asian eyes at all times after surgery. Tear film stability and volume were significantly reduced before surgery and at all times after surgery in Asian eyes. Ocular surface fluorescein staining was greater in Asian eyes before surgery and at all times after surgery. Compared with Caucasian eyes, tear secretion was significantly reduced at one month and three months after surgery in the Asian group. Central corneal sensation was significantly reduced in Asian eyes at three and six months compared with Caucasian eyes.

Asian eyes had a slower recovery to pre-operative values for some of the pre-operative dry eye parameters (Table 6). In Asian eyes, dry eye symptoms were more prevalent compared to pre-operative values at all times after surgery. In Caucasian eyes, the prevalence of dry eye symptoms was significantly increased at months 1, 3 and 6 after surgery compared to pre-operative values. Ocular surface staining was significantly increased at all times after surgery in Asian eyes but increased only at week 2 after surgery in Caucasian eyes. The PRT test was significantly reduced from pre-operative values at week 2 in Caucasian eyes and week 2, month 1 and month 3 in Asian eyes. Corneal sensation recovered to pre-operative levels by month 6 in Caucasian eyes whereas in the Asian group the recovery of corneal sensation did not occur until month 12.

Variable	Asian n = 54 (6%)	Caucasian n = 878 (94%)	*p* value*
Age ± SD (years)	34 ± 8	36 ± 9	NS§
% Female	73	55	p = 0.006
Attempted spherical equivalent correction ± SD (D)	-5.32 ± 2.28	-4.00 ± 2.23	p < 0.001
Attempted spherical correction ± SD (D)	-5.21 ± 2.23	-3.60 ± 2.26	p <0.0
Attempted cylinder correction ± SD (D)	-0.77 ± 0.73	-0.89 ± 0.95	NS
Ablation depth ± SD (µm)	76 ± 29	58 ± 26	p < 0.001
Mean pre-op keratometry ± SD (D)	44.69 ± 1.68	44.60 ± 1.93	NS
% Contact lens wear pre-op	95	78	p = 0.002
% Soft lens wearers	92	94	NS
Length of time wearing contact lens ± SD (years)	11 ± 9	11 ± 8	NS
% Diagnosed with dry eye	29	25	NS
% Receiving pre-treatment	37	30	NS

* Based on a comparison between Asian and Caucasian groups
§ NS = not significant at the 5% level

Table 2. Comparison of pre-operative demographics and tear film and ocular surface variables in Asian and Caucasian eyes (all subjects included)

Variable	Asian n = 54	Caucasian n = 878	*p* value*
Incomplete flap	0	1 (0.1%)†	NS§
Intra-operative epithelial defect	2 (3.6%)	31 (3.5%)	NS
Complete flap	0	1 (0.1%)	NS
Interface inflammation (grade 1-2)	6 (10.7%)	90 (10.3%)	NS
Interface inflammation (grade 3-4)	0	11 (1.3%)	NS
Epithelial ingrowth	0	10 (1.1%)	NS
Loss of best corrected acuity of ≥ 1 line	0	1 (0.1%)	NS

* Based on a comparison between Asian and Caucasian groups
† Number of subjects experiencing the complication
§ NS = not significant at the 5% level

Table 3. Comparison of inter-operative and post-operative complications in Asian and Caucasian eyes

DISCUSSION

To our knowledge, this is the first study that directly compares LASIK outcomes in Asian and Caucasian eyes. This study has demonstrated that Asian patients have a significantly increased risk of experiencing chronic dry eye after LASIK. It also suggests that the dry eye after LASIK is more severe and more sustained in Asian compared to Caucasian patients. These findings are due, at least in part, to Asian eyes having higher myopic corrections and therefore requiring greater refractive

Pre-operative variable	Asian patients with chronic dry eye n = 15 (28%)	Asian patients no chronic dry eye n = 39 (72%)	*p* value*
% Female	87	68	p = 0.05
Age ± SD (years)	33 ± 9	34 ± 8	NS§
Pre-operative spherical equivalent of refraction ± SD (D)	-5.59 ± 1.81	-5.78 ± 2.38	NS
Total ablation depth ± SD (µm)	75 ± 26	80 ± 30	NS
% Contact lens wear	88	95	NS
Duration of contact lens wear ± SD (years)	11 ± 8	13 ± 8	NS
% Dry eye symptoms	38	11	p = 0.002
Schirmer 1 test ± SD (mm/5 mins)	8 ± 4	16 ± 8	p = 0.01
PRT test ± SD (mm/15 s)	15 ± 8	18 ± 7	p = 0.02
FBUT ± SD (s)	4 ± 3	7 ± 3	p = 0.04
Corneal sensation ± SD (mm)	5.3 ± 1.3	5.6 ± 1.1	NS
Staining score ± SD	1.3 ± 2.5	0.1 ± 0.3	p = 0.002

* Based on a comparison between Asian patients with and without chronic dry eye
§ NS = not significant at the 5% level

Table 4. Association of chronic dry eye after LASIK in Asian eyes with pre-operative variables

Pre-operative variable	Asian n = 48	Caucasian n = 407	*p* value*
% Female	74	60	p = 0.04
Age ± SD (years)	35 ± 8	36 ± 9	NS§
Pre-operative spherical equivalent of refraction ± SD (D)	-5.62 ± 2.25	-5.66 ± 2.07	NS
Total ablation depth ± S (mm)	77 ± 29	78 ± 21	NS
% Contact lens wear	90	89	NS
Length of time in contact lens wear ± SD (years)	11 ± 7	12 ± 9	NS
% Diagnosed with dry eye	27%	22%	NS

* Based on a comparison between Asian and Caucasian groups
§ NS = not significant at the 5% level

Table 5. Patient demographics of ablation depth matched Asian and Caucasian subgroups

ablations to achieve emmetropia. We have previously demonstrated deeper stromal ablations to be a risk factor for chronic dry eye after myopic LASIK.[25] Deeper stromal ablations result in a slower return of corneal sensation to levels observed before surgery.[5,26] This loss of sensory innervation has been identified as one of the leading causes of tear film and ocular surface anomalies after LASIK surgery.[3,7,9,27]

After controlling for surgical ablation depth, other pre-operative characteristics of our Asian group could predispose this group to a higher likelihood of developing chronic post-LASIK dry eye. The Asian group had significantly more females, more contact lens wearers, lower pre-operative tear volume, less tear film stability and greater pre-operative ocular surface staining scores compared to the Caucasian group. All of these factors have been associated with a delayed recovery of corneal sensation to pre-operative levels.[4,5,9,11,25] Indeed, corneal sensation was decreased in the Asian group compared to the Caucasian group at all times, with these differences being significant at months 3 and 6 after surgery.

Additionally, anatomical differences between the Asian and Caucasian eye may produce a more severe and sustained post-LASIK dry eye. The prevalence of dry eye symptoms and diagnosed dry eye in the general population appears to be greater in Asians than in Caucasians. For example, the dry eye prevalence determined by diagnostic criteria of chronic dry eye symptoms, ocular surface staining and tear film instability or insufficiency in Japanese patients presenting to an ophthalmology clinic was 17 per cent.[28] Australian and Danish studies using similar dry eye diagnostic criteria to the Japanese study gave dry eye prevalence of 11 per cent and eight per cent, respectively.[29,30] Self-reporting of one or more dry eye symptoms experienced often or all the time occurred in 33 per cent of 598 Japanese patients[31] and 18 per cent of 1,548 Australian subjects.[29]

In elderly patients (65 years or older), dry eye symptoms are also more prevalent in Asian participants. The prevalence of self-reported dry eye symptoms occurring often or constantly was 34 per cent in 1,361 elderly Taiwanese residents[32] and 15 per cent in 2,420 elderly US residents.[33] A large scale study involving nearly 39,876 participants in the US Women's Health Study aged 45 to 84 years, determined that compared to Caucasians, Asian participants were more likely to report severe dry eye symptoms (odds ratio 1.77, confidence interval 1.17-2.69).[34] While several authors have commented on the greater prevalence of dry eye in Asian eyes, they have been unable to offer any real explanation other than to state that the differences may be due to racial and/or environmental

factors and that further research is required.[32,34]

Few published studies have compared dry eye parameters between Asian and Caucasian subjects. Cho and Brown[19] found that Asians (Hong Kong Chinese) had significantly lower FBUT (mean eight seconds) compared to 11 to 15 seconds for Caucasian eyes. These researchers attributed the lower tear film stability in Asian eyes to differences in the eyelid anatomy and their interactions with the tear film.[19] No significant differences in tear volume measured by the PRT test were found between young normal non-contact lens wearing Asian (Japanese) and Caucasian (US) eyes, although the Japanese group had a lower mean PRT test value (18.8 ± 8.6) versus. (23.9 ± 9.5).[35] We also found that our Asian patients had significantly lower PRT and FBUT than our Caucasian patients at all times before and after surgery.

Blink rates and completeness of blinking can significantly affect tear film dynamics and ocular surface health.[20,29] Differences in blink rates between Asian and Caucasian eyes have not been evaluated but it is our observation that our Asian patients, both before and after surgery, have a lower blink rate and a greater tendency to incomplete blinking. This would produce the characteristic band of inferior staining observed in our Asian patients with chronic post-LASIK dry eye (Figures 1 and 2).

We feel that the blinking and lid surfacing anomalies observed in Asian eyes are due to anatomical differences in the eyelid and orbit, possibly exacerbated by long-term contact lens wear, which is acknowledged to cause blinking anomalies,[20] and the delayed return to pre-operative values for corneal sensation in Asian eyes. Toda and colleagues[10] found that blink rates after LASIK were reduced at months 3, 6 and 12 after LASIK in their Japanese subject group. To date, no published study has evaluated blink rate in Caucasians after LASIK. Therefore, further studies to compare blink rates in Asians and Caucasians before and after LASIK are warranted.

Surgical trauma when cutting the flap is another potential factor contributing to

Dry eye assessments	Time from surgery	Asian n = 48	Caucasian n = 407	p value*
% Dry eye symptoms	Pre-op	23	20	NS†
	Week 2	51‖	29	p < 0.001
	Month 1	50‖	32	p = 0.007
	Month 3	48‖	38	p = 0.04
	Month 6	55‖	39	p = 0.001
	Month 12	43‖	29	p = 0.009
FBUT ± SD (seconds)	Pre-op	6 ± 3	8 ± 4	p = 0.02
	Week 2	3 ± 3§	6 ± 3§	p = 0.02
	Month 1	3 ± 3§	6 ± 3§	p = 0.06
	Month 3	4 ± 3	6 ± 5	p = 0.03
	Month 6	4 ± 3	7 ± 3	p = 0.02
	Month 12	4 ± 2	7 ± 5	p = 0.006
PRT ± SD (mm/15s)	Pre-op	17 ± 8	20 ± 8	p = 0.01
	Week 2	14 ± 7§	16 ± 8§	p = 0.04
	Month 1	12 ± 9§	18 ± 7	p = 0.003
	Month 3	13 ± 5§	18 ± 8	p = 0.006
	Month 6	16 ± 8	19 ± 8	p = 0.06
	Month 12	19 ± 7	24 ± 8	p = 0.005
Schirmer 1 ± SD (mm/5 min)	Pre-op	15 ± 8	16 ± 8	NS
	Month 1	6 ± 8§	11 ± 8§	p = 0.009
	Month 3	9 ± 5§	12 ± 11§	p = 0.03
	Month 6	13 ± 6	15 ± 10	NS
	Month 12	14 ± 10	16 ± 11	NS
Staining score ± SD	Pre-op	0.5 ± 1.5	0.3 ± 1.0	p = 0.04
	Week 2	1.7 ± 3.0‖	0.6 ± 1.8‖	p < 0.001
	Month 1	1.1 ± 2.7‖	0.5 ± 1.7	p = 0.008
	Month 3	0.9 ± 1.8‖	0.5 ± 1.7	p = 0.03
	Month 6	1.1 ± 1.9‖	0.4 ± 1.4	p = 0.005
	Month 12	1.0 ± 2.1‖	0.4 ± 1.4	p < 0.001
Corneal sensation ± SD (mm)	Pre-op	5.3 ± 0.6	5.4 ± 1.0	NS
	Week 2	0.3 ± 1.6§	0.5 ± 1.8§	NS
	Month 1	1.0 ± 1.9§	1.1 ± 2.0§	NS
	Month 3	2.2 ± 2.1§	3.4 ± 2.0§	p = 0.03
	Month 6	3.8 ± 2.0§	4.9 ± 1.8	p = 0.04
	Month 12	4.7 ± 2.1	5.1 ± 1.5	NS

* Based on a comparison between Asian and Caucasian patient groups
† NS = not significant at the 5% level
‖ Significantly increased (at the 5% level) from pre-operative value
§ Significantly decreased (at the 5% level) from pre-operative value

Table 6. Comparison of dry eye assessments before and after myopic LASIK surgery in Asian and Caucasian groups matched for pre-operative refractive target and total laser ablation depth

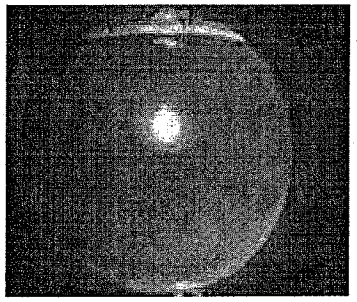

Figure 1. Chronic LASIK dry eye in a female Asian patient at nine months post LASIK for -11 D myopic correction. There is significant inferior punctate epitheliopathy and a less severe band of staining superior to the central ablation zone.

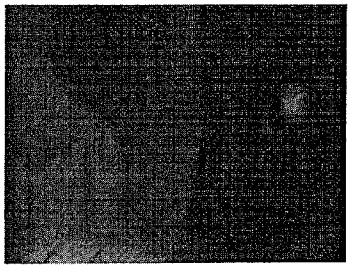

Figure 2. Significant inferior punctate epitheliopathy in an Asian eye with inferior entropion and trichiasis one month post-LASIK. Contact lens wear before surgery masked the condition.

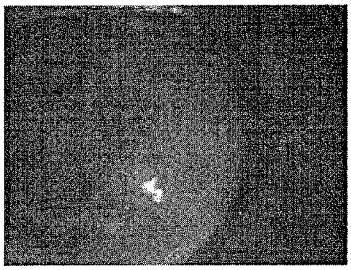

Figure 3. Diffuse staining in a female Asian patient at week 2 after LASIK for -6 D myopic correction. The patient had not been using post-operative lubrication routinely.

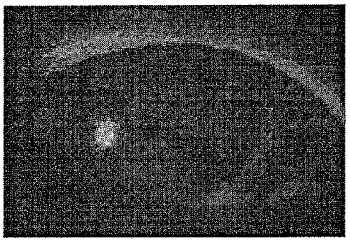

Figure 4. Superior entropion and trichiasis masked by contact lens wear in a pre-operative LASIK candidate. The patient was advised to remain in contact lenses or consider entropion repair prior to undergoing any form of keratorefractive surgery.

ocular surface damage and dry eye after LASIK.[36] In general, Asian eyes have a shallower orbit, smaller vertical orbital dimensions and differences in the upper eyelid anatomy compared to Caucasians. Asian eyes also have narrower palpebral fissures.[37,38] These factors can predispose Asian eyes to greater likelihood of flap cut problems.[38] Asano-Kato and co-workers[39] found that Asian eyes were more disposed to problems with suction with the microkeratome. They concluded that the narrow palpebral fissures commonly found in Asian populations might be a risk factor for insufficient fixation of a microkeratome in LASIK. Although our Asian patients did not experience a higher incidence of flap cut complications, our surgeon did find that intra-operative preparation for the flap cut took longer for Asian eyes compared with Caucasian eyes, due to these eyelid and orbital issues. Longer intra-operative times and a tight fit with the suction ring and keratome, even in the absence of flap cut complications, could add to the intra-operative damage to the ocular surface and the perilimbal goblet cell loss and be a contributing factor to the high degree of ocular surface staining seen after LASIK in Asian patients (Figure 3).

Epiblepharon and entropion can be features of Asian eyelids and, in severe cases, are associated with trichiasis and corneal punctate epithelial erosions.[37] Contact lens wear will mask the effects of trichiasis (Figures 4) and these patients may need to consider eyelid surgery to correct the eyelid anomalies before LASIK if significant trichiasis and punctate erosions are present, or alternatively remain in their contact lenses if ocular health permits.

The greater prevalence, duration and severity of dry eye in our Asian group is concerning, particularly given that we employ intensive ocular surface management strategies before, during and after surgery in an attempt to reduce the incidence and severity of LASIK induced dry eye,[8,35,36] and given that the prevalence and severity of myopia in Asian eyes is increasing. Asian LASIK candidates with increased risk of developing dry eye (females, dry eye before surgery, higher attempted corrections and long-term contact lens wearers) should be counselled pre-operatively regarding their increased risk of developing chronic dry eye after LASIK and alternative corrective options should be considered. It may be prudent for Asian patients who are safely and comfortably wearing contact lenses to remain in their contact lenses or to consider photorefractive keratectomy which has a lower long-term incidence of chronic dry eye symptoms and signs.[1,7,40]

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EVIDENCE - 8

antibiotics. In one eye, a scarring process slightly decreased BSCVA.

Our cases illustrate that even when LASIK is performed in a sterile manner, as in intraocular surgery, a risk of pneumococcal keratitis still remains. Patients need to be informed of this potential risk before LASIK. Surgeons should be alert in such cases to provide prompt treatment. When appropriate therapy is started early, the clinical picture improves within days and achieved BSCVA is ≥20/25.

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Retinal Phlebitis After LASIK

Jane-Ming Lin, MD; Yi-Yu Tsai, MD

ABSTRACT

PURPOSE: To report a case of retinal phlebitis with cystoid macular edema in both eyes 8 weeks after LASIK.

METHODS: A 30-year-old woman underwent bilateral myopic LASIK. Eight weeks postoperatively, the patient experienced blurred vision in the left and right eyes. Fundus examination showed focal whitish patches in the parafoveal and juxtafoveal areas and lack of foveal reflex in both eyes. A diagnosis of retinal phlebitis with cystoid macular edema was made, which was treated with oral corticosteroids with tapering dose.

RESULTS: Visual acuity returned to normal and the whitish fundus patches decreased in number and size in both eyes.

CONCLUSIONS: Surgeons should be aware of potential risks and retinal complications associated with LASIK. [*J Refract Surg*. 2005;21:501-504.]

The increasing number of LASIK surgeries for myopia has led to an awareness of the potential hazards and retinal complications of this procedure. Reported posterior segment complications include rhegmatogenous retinal detachment,[1] choroidal infarction,[2] macular, submacular, or premacular hemorrhage,[1,3] macular hole,[4] central or branch retinal vein occlusion,[5] retinal nerve fiber layer defects,[6] optic neuropathy,[7] and cystoid macular edema.[8]

We report a 30-year-old woman who underwent bilateral myopic LASIK. Retinal phlebitis with cystoid macular edema developed in both eyes 8 weeks postoperatively. Visual acuity returned to normal after treatment with oral steroids.

CASE REPORT

A 30-year-old woman with an insignificant medical

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and ocular history underwent bilateral myopic LASIK. Before LASIK, refractive error was −7.50 −3.25 × 15° in the right eye and −8.00 −2.75 × 140° in the left eye. Best spectacle-corrected visual acuity (BSCVA) in both eyes was 20/20. Postoperative uncorrected visual acuity (UCVA) was 20/20 in both eyes.

Eight weeks after surgery, the patient experienced onset of blurred vision in the left eye. Three days later, the same symptom occurred in the right eye.

On initial evaluation, BSCVA was 20/100 in the right eye and 16/200 in the left eye. Anterior segment examination was unremarkable except for a well-healed LASIK flap and trace subepithelial haze in both eyes. Intraocular pressure (IOP) was normal. The vitreous was free of cells. Fundus examination showed several focal whitish patches in the parafoveal and juxtafoveal areas and lack of foveal reflex in both eyes (Fig 1A). Fluorescein angiography revealed late staining of the dye in the wall of the dilated venules (the left eye more than the right eye) and mild cystoid macular edema bilaterally (Fig 1B).

Visual field testing with Humphery Central 30-2 Threshold Test (Humphery Instruments, San Leandro, Calif) was normal in the right eye, but demonstrated a paracentral scotoma in the left eye. No other extraocular lesion was observed. Results of laboratory studies were normal. Therefore, diagnosis of retinal phlebitis in both eyes was made. The patient was treated with oral corticosteroids with tapering dose.

On subsequent examinations, visual acuity continued to improve. One month after treatment, UCVA was 20/30 in the right eye and 20/200 in the left eye. Best spectacle-corrected visual acuity improved to 20/20 in the right eye and 20/25 in the left eye. Whitish fundus patches decreased in number and size in both eyes. Fluorescein angiography demonstrated moderate resolution of cystoid macular edema and no venous dye staining in both eyes. Visual field in the left eye also returned to normal.

Two months after treatment, UCVA was 20/20 in the right eye and 20/30 in the left eye (BSCVA 20/20). Fundus examinations revealed faint whitish patches and normal foveal reflex in both eyes. On final examination 6.5 months after treatment, UCVA had returned to 20/20 in both eyes. Fundus examinations in both eyes were essentially unremarkable except for some mottling changes of retinal pigment epithelium at the posterior pole of the right eye (Fig 2A). Fluorescein angiography of both eyes revealed no venous dye staining or cystoid macular edema (Fig 2B).

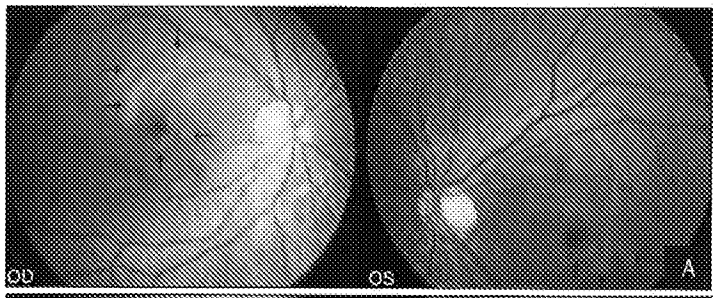
DISCUSSION

Retinal vasculitis has posed a difficult diagnostic problem for ophthalmologists for many years. It is a sight-threatening inflammatory disease with an unknown etiology and pathogenesis. Retinal veins, capillaries, and arterioles may be involved and veins are most commonly affected. It may occur as a complication of infection, neoplasm, degenerative disorders, or be associated with systemic inflammatory diseases (eg, Behçet's syndrome, sarcoidosis, uveomeningitis, HLA-B-27 related arthritis) or isolated findings.[8] In a study by Graham et al[9] of 150 patients with idiopathic retinal vasculitis, 67 (45%) patients had isolated retinal vasculitis and 83 (55%) patients had retinal vasculitis associated with systemic inflammatory disease. In our patient, we found no evidence of associated systemic inflammatory disease, infection, or neoplasm. The patient's reduction in visual acuity was not caused by myopic subretinal neovascularization or hemorrhage but by cystoid macular edema. No previous ocular disease was reported that could have explained cystoid macular edema, and no events (trauma or other inflammation) other than LASIK occurred. Therefore, we believe this patient's retinal phlebitis with cystoid macular edema may be associated with LASIK.

The rise and decompression of IOP during suction and the acoustic shock waves created by the laser might have been responsible for the retinal phlebitis seen in our patient.[1] An IOP of at least 65 mmHg is necessary to create a corneal flap with the microkeratome. During this time, the shape of the anterior segment may change rapidly and structures posterior to the suction ring are also compressed in sequence.[10,11] When the suction stops and the suction ring is released, ocular decompression leads to dynamic equatorial elongation and anterior-posterior contraction.[10] This barotrauma is analogous to what happens in closed-eye injury[12,13] and can alter delicate retinal structures, especially small vessels, and induce vitreoretinal traction at the vitreous base and posterior pole.[10,14] Sudden elevation of IOP also disturbs the retinal circulation and increases venous pressure, which results in retinal ischemia. All of these conditions may aggravate the original impaired blood-retinal barrier in highly myopic eyes and increase vascular permeability,[15] leading to the loss of integrity of tight junctions of endothelial cells.

Laser in situ keratomileusis-induced shock waves can generate up to 100 atm.[16] Although the pressure decreases steadily to values below 10 bars toward the retina,[1] we believe it may still cause mechanical stress to the retina, resulting in structural damage and intraocular inflammation. In addition, total energy and duration increase with higher refractive error and the effect of mechanical stress may be more severe in higher myopia, which has more liquefaction of the posterior vitreous gel.[17]

Of course, one case report does not prove a cause-



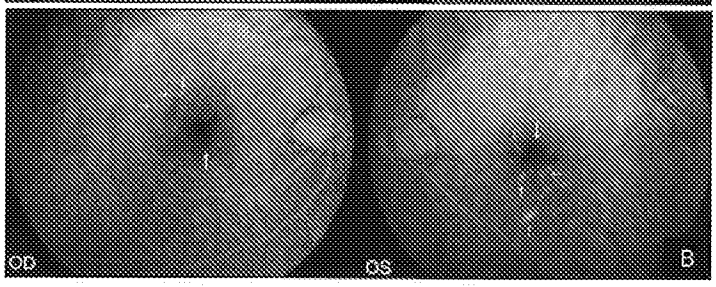
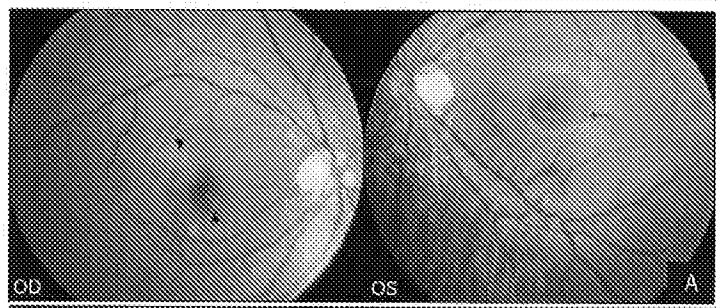


Figure 1. Fundus photograph and fluorescein angiogram 8 weeks after LASIK. **A)** Fundus photographs showed several focal whitish patches in the parafoveal and juxtafoveal areas (arrows) and lack of foveal reflex in both eyes. **B)** Late phase of fluorescein angiography revealed staining of the dye in the wall of the dilated venules (small arrows, the left eye more than the right eye) and mild cystoid macular edema bilaterally (large arrows).



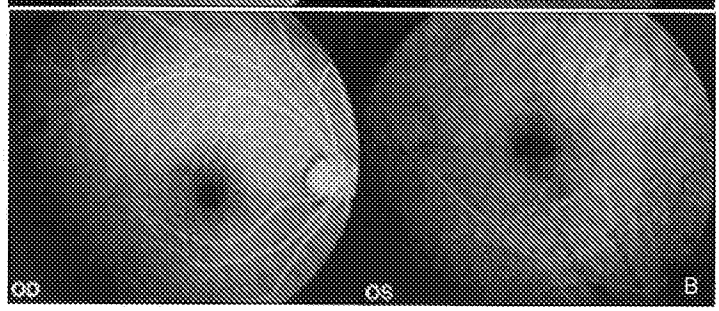


Figure 2. Fundus photograph and fluorescein angiogram 6.5 months after treatment. **A)** Fundus photographs in both eyes were essentially unremarkable except for some mottling retinal pigment epithelium at the posterior pole of the right eye (arrowhead). Normal foveal reflex was noted in the left eye (arrow). **B)** Fluorescein angiography revealed no venous dye staining or cystoid macular edema.

and-effect relationship between LASIK and retinal phlebitis. However, this report should alert ophthalmologists to the importance of determining the risk factors, performing echography of vitreous, indirect ophthalmoscopy with scleral depression, and possibly photography and fluorescein angiography of macula to determine whether the LASIK procedure itself might exacerbate the original pathologic changes of myopia.

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Decrease in Tear Secretion and Corneal Sensitivity After Laser In Situ Keratomileusis [Clinical Sciences]

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Abstract TOP

Purpose. To evaluate tear secretion and corneal sensitivity after laser in situ keratomileusis (LASIK) for the correction of myopia.

Methods. In a prospective study, 48 consecutive eyes (24 patients) underwent LASIK to correct myopia ranging from -3.5 to -12.25 diopters. Tear secretion tested by the tear function index and corneal sensitivity tested using the Cochet-Bonnet esthesiometer were evaluated preoperatively and 1 week and 1, 3, 6, and 9 months postoperatively.

Results. Tear secretion and corneal sensitivity after LASIK were reduced during the first 3 months after surgery ($p < 0.001$). Tear secretion returned to its preoperative values only after 9 months. Tear secretion and corneal sensitivity were more depressed in long-term contact lens wearers preoperatively and 6 months after surgery ($p < 0.05$).

Conclusion. In the correction of myopia, tear secretion was depressed after LASIK during the first 6 months after surgery.

After laser in situ keratomileusis (LASIK), patients usually report dry eye symptoms. Dry eye arises from a series of etiologies. 1 Normal corneal sensitivity is important to normal corneal function. The ocular surface (cornea, conjunctiva, accessory lacrimal glands, and Meibomian glands), the main lacrimal gland, and the interconnecting neural reflex loops comprise a functional unit whose parts acts together. 2 Tear secretion is in part, if not wholly, reflexive in origin. When the afferent nerves of the ocular surface (trigeminal nerve) are stimulated in a normal individual, a reflex results in immediate blinking and secretion of tears. Sensory loss causes decreased tear secretion and, when bilateral, reduces the blink rate. 3

Significantly decreased sensitivity may be caused by certain disorders, including diabetes and herpes keratitis. Contact lens wear can also induce corneal hypesthesia. [4] Various refractive surgical procedures have been associated with marked postoperative hypesthesia. [5-7] Perez-Santonja et al. [7] demonstrated a more depressed corneal sensitivity after LASIK than after photorefractive keratectomy. Only after 6 months did corneal sensitivity return to its preoperative values. In this study, we aimed to evaluate tear secretion and corneal sensitivity after LASIK for correction of myopia.

METHODS TOP

Of 24 patients who underwent LASIK, 48 consecutive eyes were prospectively studied. All procedures were performed by the same surgeon (J.M.B.C.). Patient selection criteria were age 21 to 45 years; stable myopia -3 to -13 diopters (D), astigmatism less than 2.5 D, intolerance of contact lenses or unwillingness to wear spectacles and/or contact lenses, normal anterior segment, normal peripheral retina, and no general health problems, previous ocular surgery, corneal diseases, glaucoma, or history of ocular trauma. Informed consent was obtained from all patients after they received a detailed description of the surgical procedures and their known risks.

Pre-and postoperative basic ocular examination included visual acuity, manifest and cycloplegic refraction, slit-lamp biomicroscopy, applanation tonometry, pachymetry, videokeratography, indirect ophthalmoscopy, tear secretion, and corneal sensitivity testing. Patients were asked to discontinue contact lens use 3 weeks before the surgery. Postoperative tear secretion and corneal sensitivity testing were conducted at 1 week and at 1, 3, 6, and 9 months.

All laser in situ procedures were performed with the Bausch & Lomb Hansatome microkeratome (Claremont, CA, U.S.A.) and the Keratom Multi-Scan Schwind excimer laser (Kleinostheim, Germany). The procedure was done with topical anesthesia of 0.4% oxybuprocaine. The flap diameter created by the microkeratome was 8.5 mm and its thickness was 160 µm. A 6-mm single-zone ablation was used for all of the patients. Ciprofloxacin 0.3% and fluorometholone 0.1% eyedrops were instilled four time a day for the first week.

The Schirmer values with anesthesia and the tear clearance rate [8] were measured 5 minutes after instilling a 10-µL drop of 0.5% fluorescein and 0.4% oxybuprocaine hydrochloride into the conjunctival sac. A standard Schirmer test strip then was placed for another 5 minutes. The length of the wet portion was measured and the intensity of its staining was compared with the standard strip colors for the Schirmer test with anesthesia or tear-clearance rate respectively. The tear-clearance rate was determined by the rate at which the color of the fluorescein dye faded and was graded as 1, 1/2, 1/4, 1/8, 1/16, 1/32, 1/64, 1/128, or 1/256. The tear function index (TFI) was defined as the value of the Schirmer test with anesthesia divided by the tear clearance rate. [9] All tests were conducted in a quiet room of relatively constant temperature (22°C) and humidity.

Corneal sensitivity was tested using the Cochet-Bonnet esthesiometer (Luneau, Paris, France). The instrument consists of a nylon monofilament 0.12 mm in diameter with a variable length of 0 to 62 mm so that the pressure applied to against the cornea can be 11 to 200 mg/0.0113 mm^2. The test is performed with the patient positioned at the slit-lamp. The instrument is advanced perpendicular to the corneal surface until contact is made. If the patient feels the filament, the response will be considered positive. The test was started at the maximal length, approximately 62 mm, which is the lowest possible pressure. A bend in the filament gave an objective measurement of contact. If no response was obtained at 62 mm, the length was reduced to 55 mm, and thereafter it was reduced in 5-mm increments until a positive response was obtained. At each length, three measurements were performed at the center of the cornea (inside the ablated area). The longest filament length with which a positive response was obtained from the patient was considered to be the corneal sensitivity threshold. All measurements were performed by the same observer (J.M.B.C.) before any drops were placed in the eye. We are aware that using the Cochet-Bonnet esthesiometer has limitations, particularly at the upper end of the scale. If the patients feels the filament at the maximum length (62 mm), the response will be considered positive at 62 mm, when the real corneal sensitivity could be 62 mm or higher. However, normal corneal sensitivity is usually approximately 62 mm, and the Cochet-Bonnet esthesiometer was the one most used instruments in previous studies. [5-7]

Both parametric and nonparametric statistical analyses were done, based on the distribution of the data under consideration. Measurements for right and left eyes of each subject were averaged for the analysis. Differences for continuous variables were tested with the Student *t* test for normally distributed data, and the Mann-Whitney and Wilcoxon rank sum tests for non-normally distributed data. Differences for categoric variables were tested with the Fisher exact test for independence. Correlations between continuous variables were obtained using the Spearman correlation coefficient. Differences were considered statistically significant when p values were less than 0.05.

RESULTS TOP

The mean patient age was 29.3 ± 6.6 years (mean ± SD). Of all, 14 patients were female and 10 patients were

male. Both eyes of the patients were included in the study. Mean preoperative refraction was -7.6 ± 2.3 D (range, -3.5 to -12.25 D) and the mean preoperative pachymetry was 535 ± 31 μm (range, 484 to 572 μm). All patients were available at each of the postoperative follow-ups. Of all, 12 patients were long-term contact lens wearers (more than 5 years) and 12 were not contact lens wearers. Mean preoperative and postoperative TFI and corneal sensitivity values are shown in Table 1.

Table 1

TABLE 1. *Mean ± SD preoperative and postoperative TFI and corneal sensitivity* 0.001.

There was an important decrease in TFI at 1 week and 1 month ($p < 0.001$) after surgery. TFI showed some recovery at 3 months, although the difference was still significant ($p < 0.001$). At 6 months, TFI nearly returned to its preoperative values ($p = 0.07$). TFI returned to preoperative values at 9 months after surgery ($p = 0.77$).

There was a deep decrease in corneal sensitivity at 1 week and 1 month ($p < 0.001$) after surgery. Corneal sensitivity showed some recovery at 3 months ($p < 0.001$) and returned to nearly preoperative values at 6 months after surgery ($p = 0.20$). At 9 months, corneal sensitivity returned to its preoperative values ($p = 0.98$). A statistical correlation was found between TFI and corneal sensitivity before and after surgery ($p < 0.05$). No statistical correlation was found between depth of ablation (as determined by attempted correction) and postoperative TFI and corneal sensitivity at any point of the follow-up ($p > 0.05$). No statistical correlation was found between age and postoperative TFI and corneal sensitivity at any point of the follow-up ($p > 0.05$).

There was no significant difference in preoperative refraction, pachymetry, and gender between the long-term contact lens wearers and noncontact lens wearers. There was a significant difference in preoperative TFI and corneal sensitivity when long-term contact lens wearers and noncontact lens wearers were compared (TFI: 231 ± 514 vs. 272 ± 505, $p < 0.05$; corneal sensitivity: 58.7 ± 5.8 vs. 62.0 ± 0.0, $p < 0.05$). No differences were found between both groups at 1 week and at 1 and 3 months. However, 6 months after surgery, TFI and corneal sensitivity values were lower in the long-term contact lens wearers than in the noncontact lens wearers (TFI: 220 ± 485 vs. 248 ± 345, $p < 0.05$; corneal sensitivity: 56.5 ± 7.1 vs. 59.1 ± 3.5, $p < 0.05$). No differences were observed between both groups at 9 months after surgery.

DISCUSSION TOP

The primary function of tears is to serve as a first line of defense to protect the ocular surface against microbial and toxic agents. Tears supply necessary ingredients (e.g., vitamin A and lysozymes) and remove harmful substances (e.g., inflammatory cytokines and allergens). Any imbalance between tear secretion, evaporation and drainage can impair the precorneal tear film and, thus, can result in dry eye. Dry eyes may be assigned to two major classes: tear-deficient dry eye and evaporative dry eye. [1] Tear-deficient dry eye requires the demonstration of defective lacrimal production. Secreted by the lacrimal gland and swept over the ocular surface by blinking, tears either evaporate or migrate to the inner canthus and ultimately to the nose. Tear dynamics thus are determined by three factors: production or secretion, evaporation, and drainage. Although we cannot measure tear secretion independently and directly, the TFI incorporates the Schirmer and the tear clearance rate tests and eliminates the influence by the forces of tear drainage. The higher the TFI, the higher tear secretion. [9]

Corneal sensitivity is mediated by axon terminals of the long ciliary nerves. Seventy to eighty large radial branches enter the cornea at the midstromal level. As these nerves course to the center of the cornea, they branch horizontally and vertically, giving rise to the dense subepithelial plexus beneath Bowman layer. [10] Normal corneal sensitivity is essential to normal structure and function. Although some variations in corneal sensitivity are normal, significantly decreased sensitivity may be caused by diabetes, herpes simplex, contact lenses, or by some surgical and medical ocular treatments. [4] Corneal hypesthesia compromises the protective blinking reflex, delays epithelial wound healing, and is associated with decrease tear secretion. Stimulation of the ocular surface initiates neural signals, resulting in aqueous tear secretion. [2] Corneal sensitivity is very acute, centrally processed, and interpreted solely as pain. [11] The so-called basal tearing results from continuous stimulation of the corneal surface by environmental factors, even though these signals occur below the level of perception in normal individuals. [3]

Several corneal and refractive surgical procedures have been associated with a marked loss of normal sensitivity. A return of corneal sensitivity to normal levels within 12 months after penetrating keratoplasty has been reported. [12] Radial keratotomy can also reduce corneal sensitivity as long as 1 year postoperatively. [5] After photorefractive keratectomy, patients recover corneal sensitivity within the first 3 postoperative months. [13]

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LASIK to correct myopia is a new technique that has generated high expectations among refractive surgeons. Preliminary studies found that LASIK offers excellent results in the correction of moderate and severe myopia, with few complications in experienced hands. [14-16] In LASIK, a corneal flap (with the corneal epithelium, Bowman layer, and anterior stroma) is created using a microkeratome. During this procedure, the superficial stromal nerves are cut in the flap margin, and the nerves in the stromal bed under the flap are subsequently exposed to excimer laser photoablation. Linna et al. [17] have shown in rabbit cornea that at 5 months after LASIK, the epithelial, subepithelial, and anterior stromal innervation had gained an almost normal nerve density and architecture. Perez-Santonja et al. [7] in a series of 17 eyes after LASIK for the correction of myopia, found that corneal sensitivity was nearly normal 6 months after surgery. Our results show a deep decrease in corneal sensitivity at 1 week and at 1 and 3 months after LASIK. Although some recovery was present at 6 months, corneal sensitivity returned to its preoperatively values at 9 months.

Reduced corneal sensitivity facilitates dry eye by two mechanisms: sensory loss causes decreased tear secretion [3] and, when bilateral, reduces the blink rate. Infrequent blinking is associated with ocular drying due to increased tear evaporation. Therefore, dry eye in LASIK may be assigned to the two major classes: tear-deficient and evaporative dry eye. [1] Our study shows that tear secretion after LASIK for the correction of myopia is reduced during the first 6 months after surgery and that it returned to its preoperative values only after 9 months. Comparing long-term contact lens wearers with noncontact lens wearers, corneal sensitivity and tear secretion was more depressed preoperatively and at 6 months after LASIK in long-term contact lens wearers, although no differences were found at 9 months. Loss of corneal sensitivity is a feature of contact lens wear and it has been proposed as a mechanism for dry aye associated with long-term contact lens wear. [18] Alternative suggestions for the mechanism of decreased tearing may also relate to changes in the shape of the ocular surface and its relationship to the upper lid possibly resulting in increased evaporative tear loss. In conclusion, in the correction of myopia, tear secretion is reduced after LASIK. Only after 9 months is tear secretion recovered. These results indicate the importance of artificial tears usage in the LASIK patients.

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